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THE BRITISH JOURNAL OF RADIOLOGY

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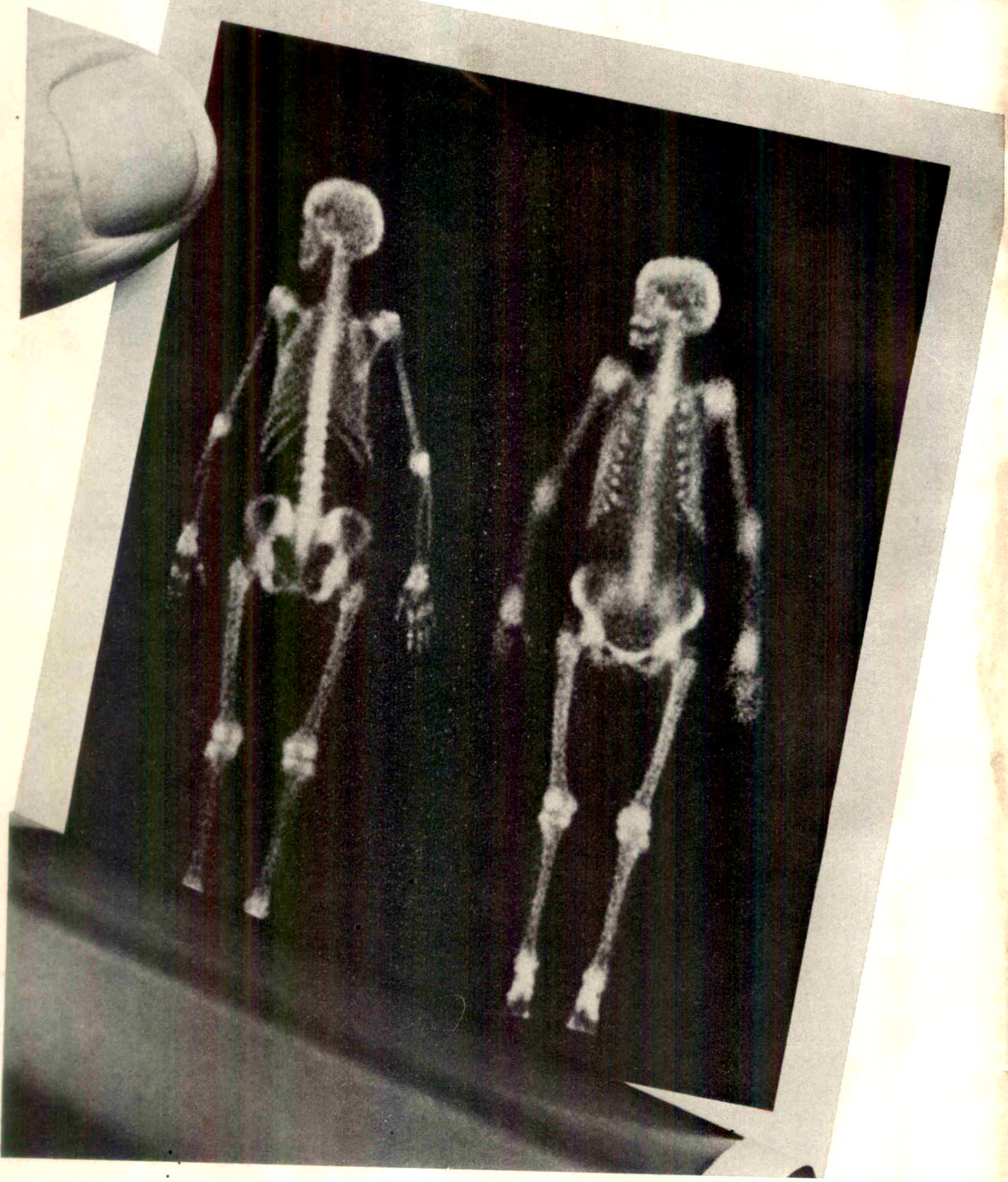

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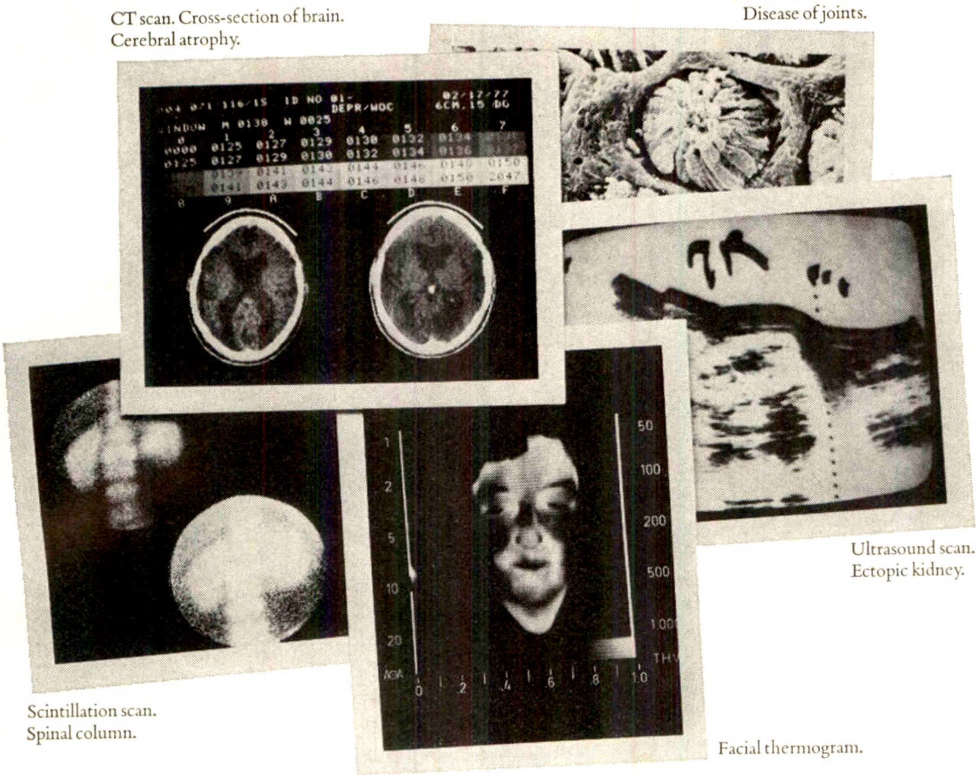

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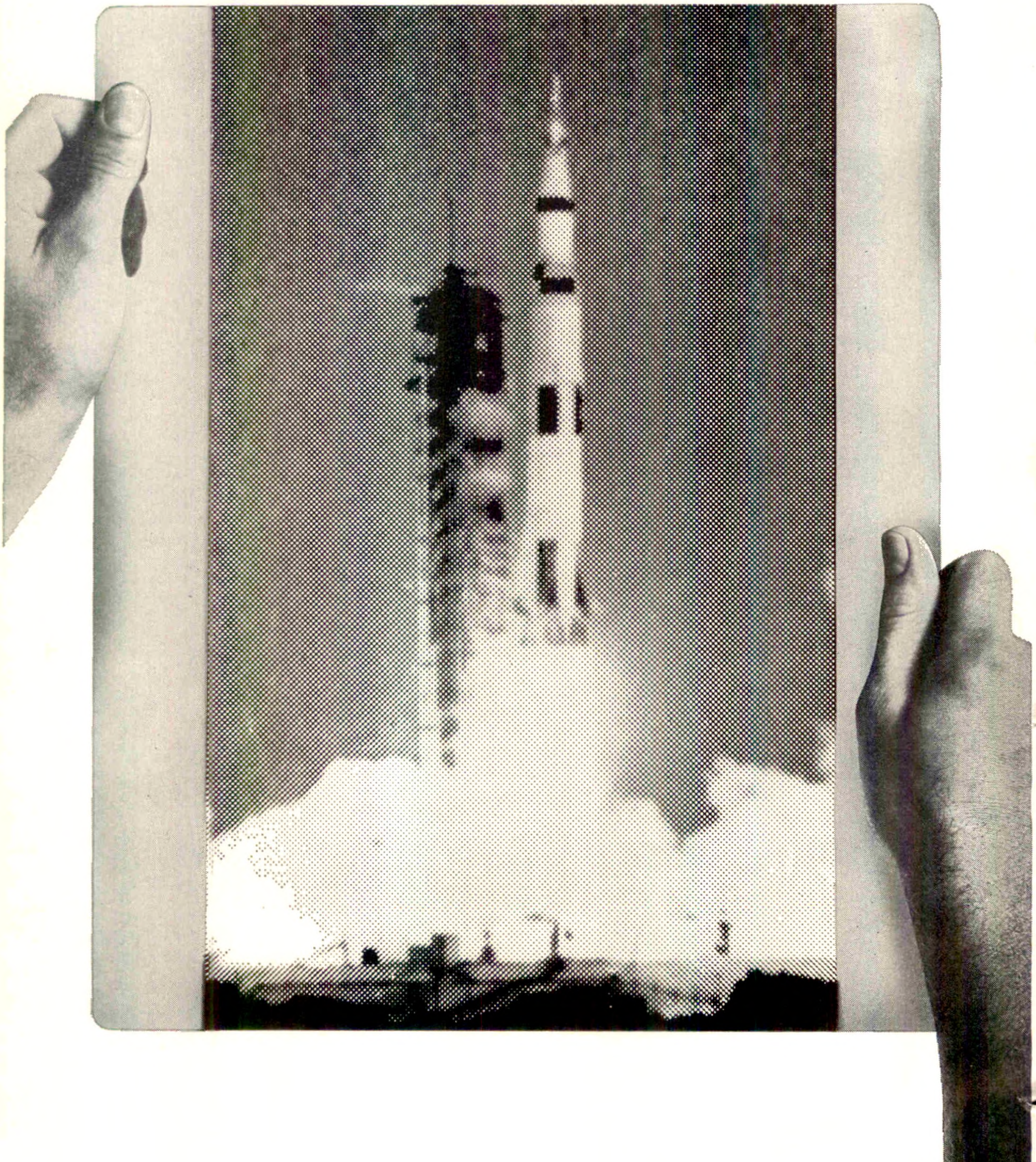

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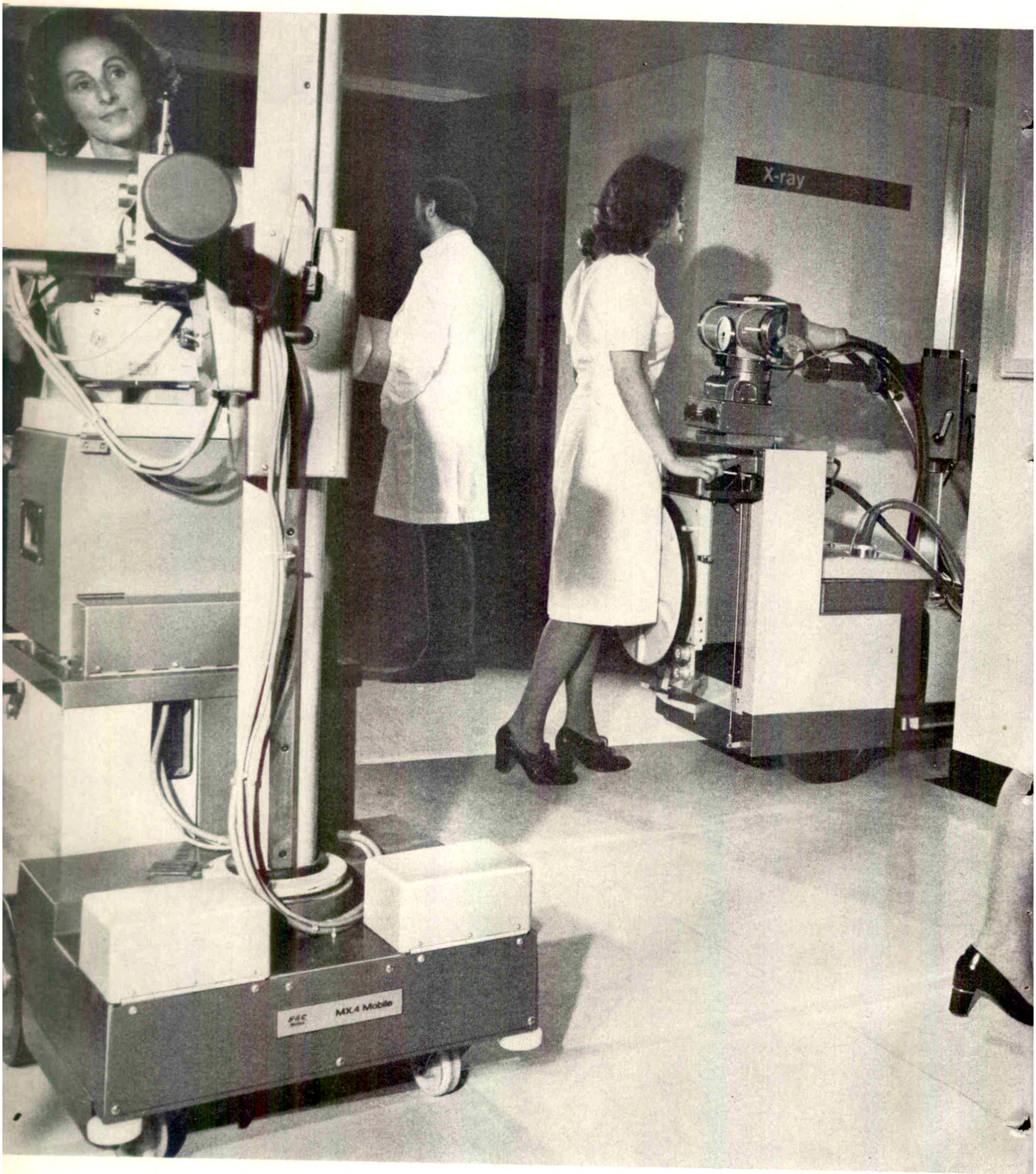

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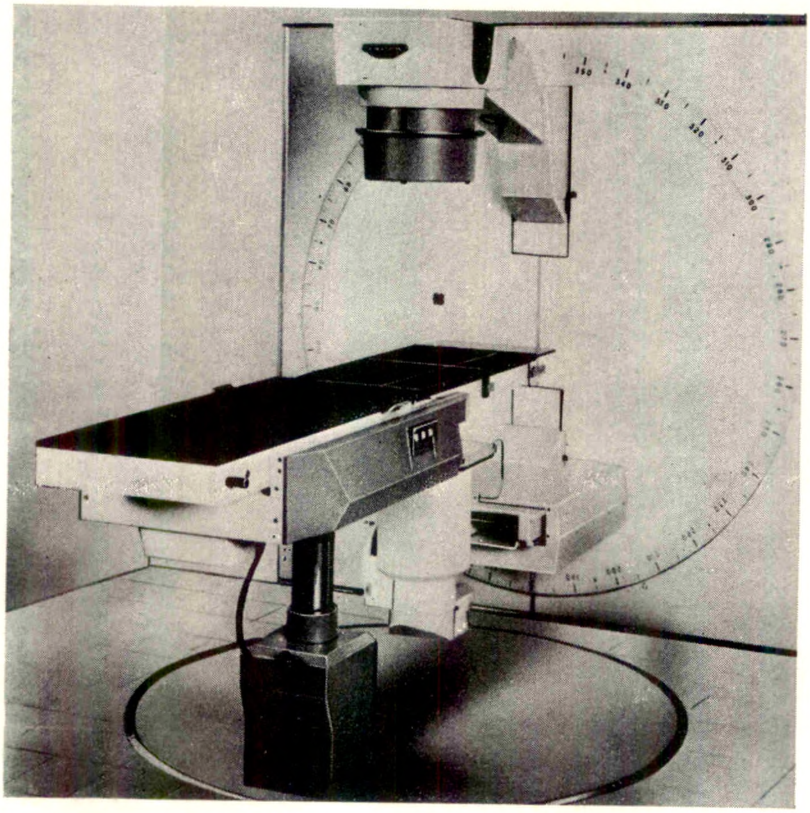

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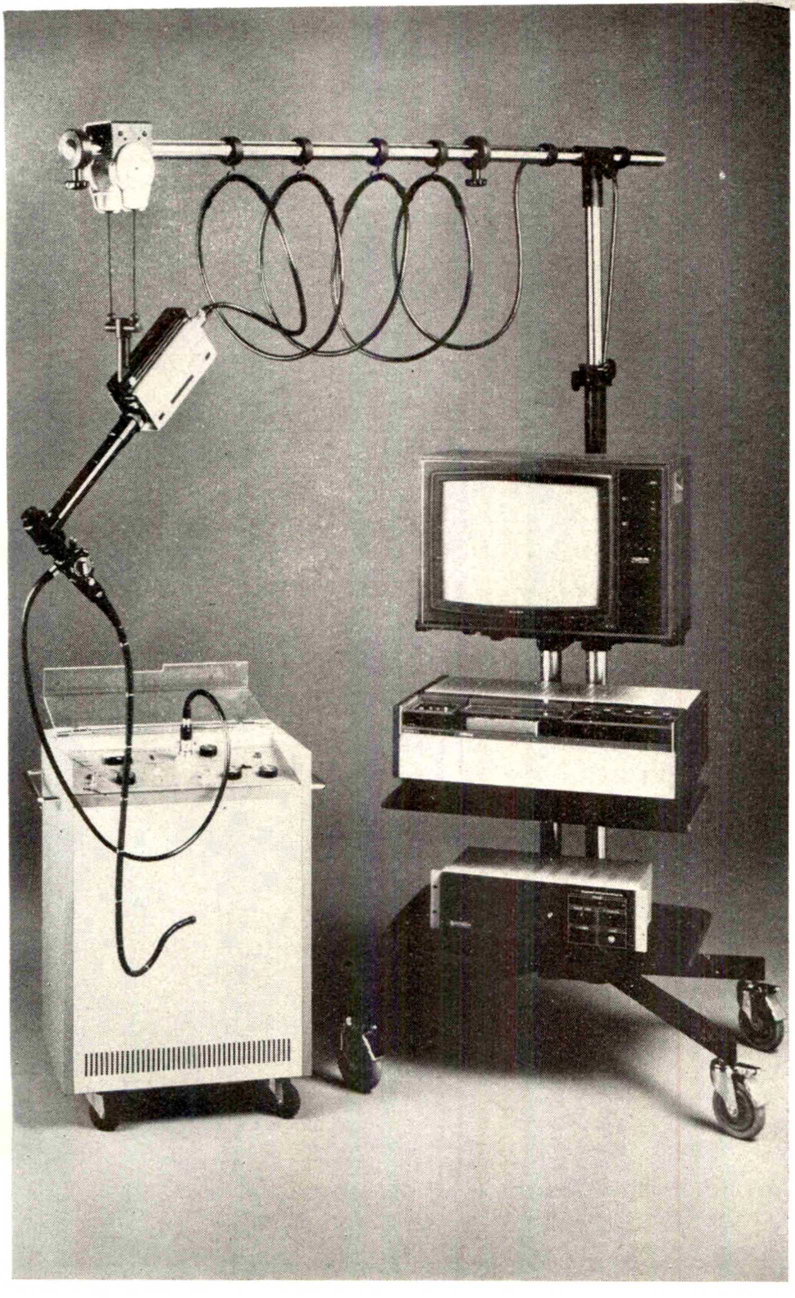

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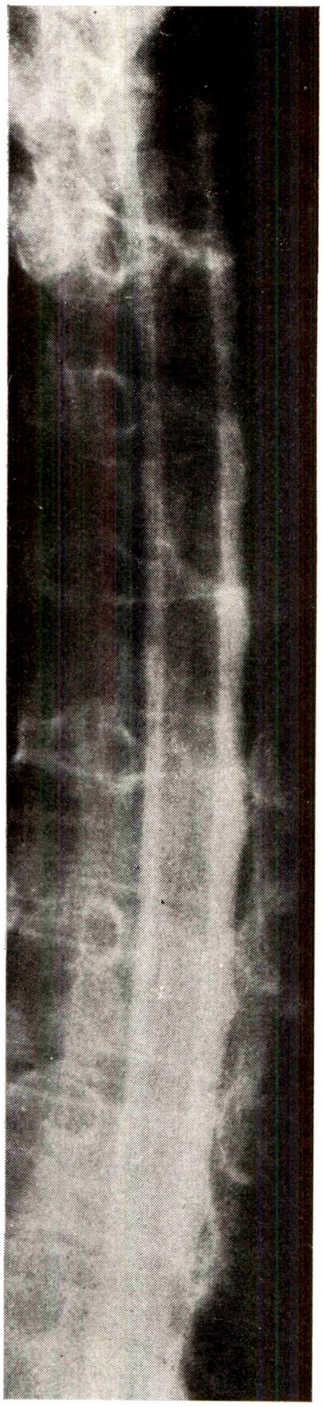

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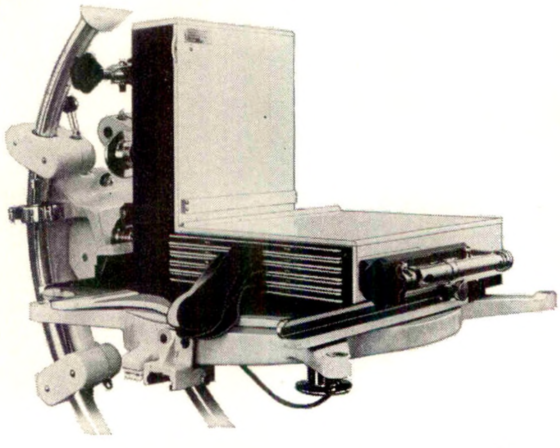

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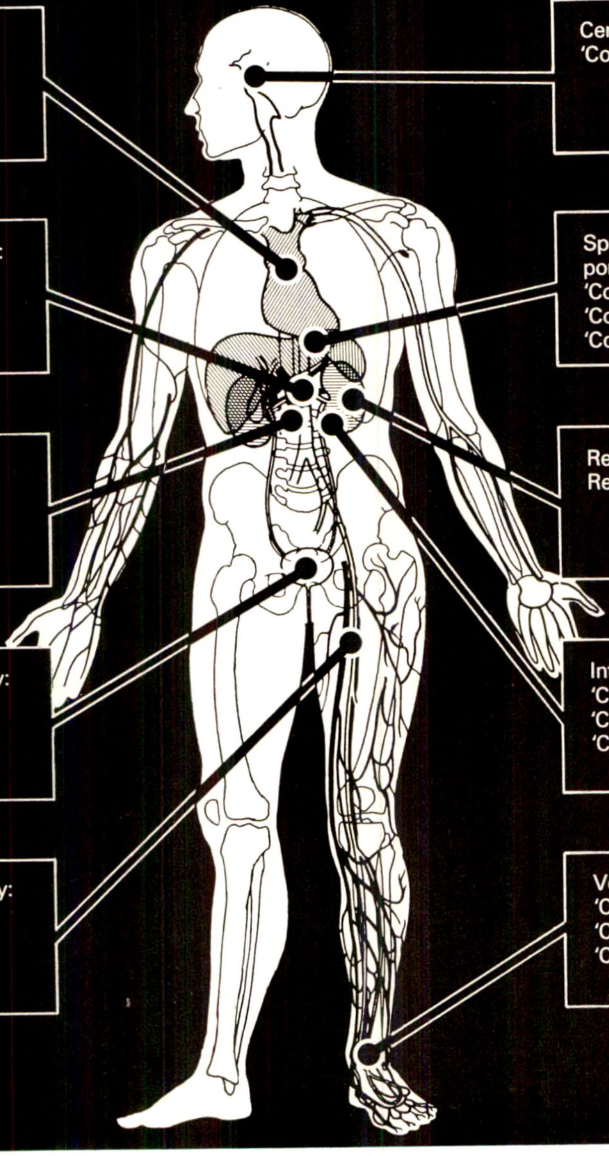

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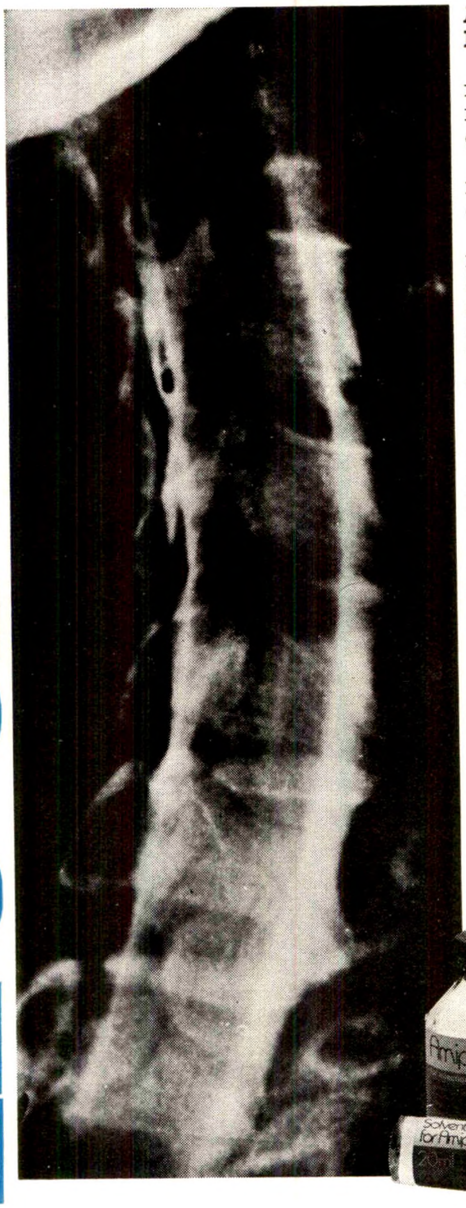

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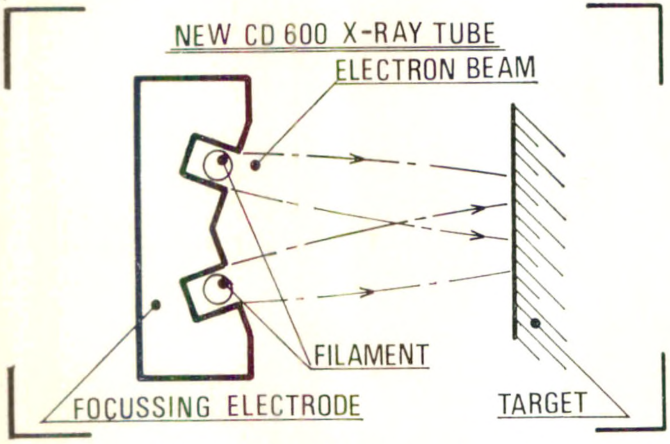

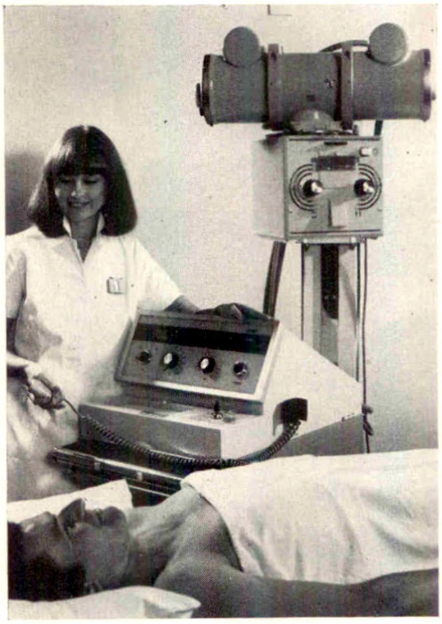

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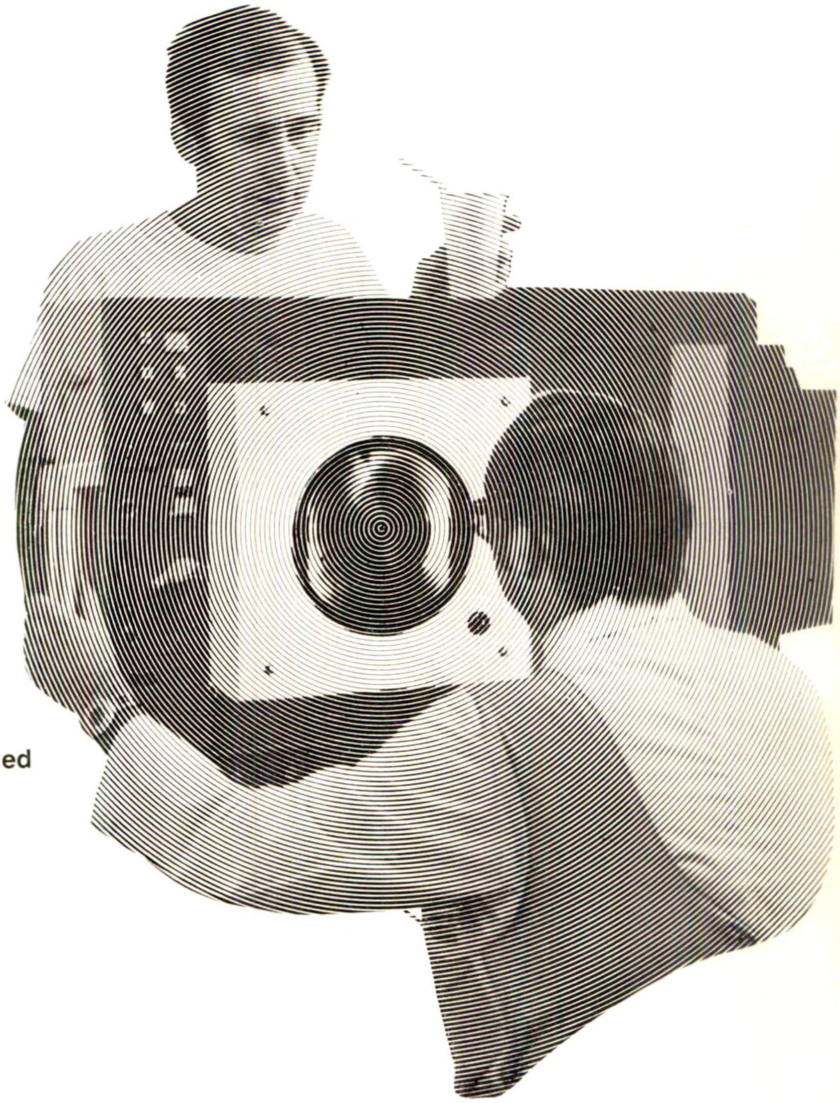

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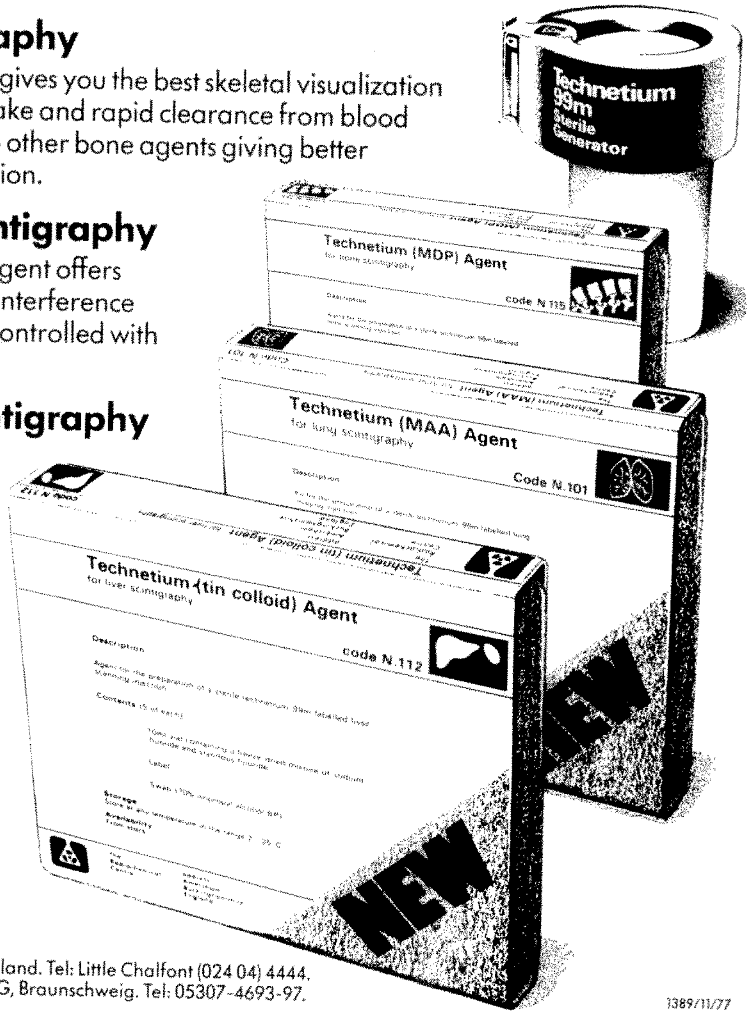

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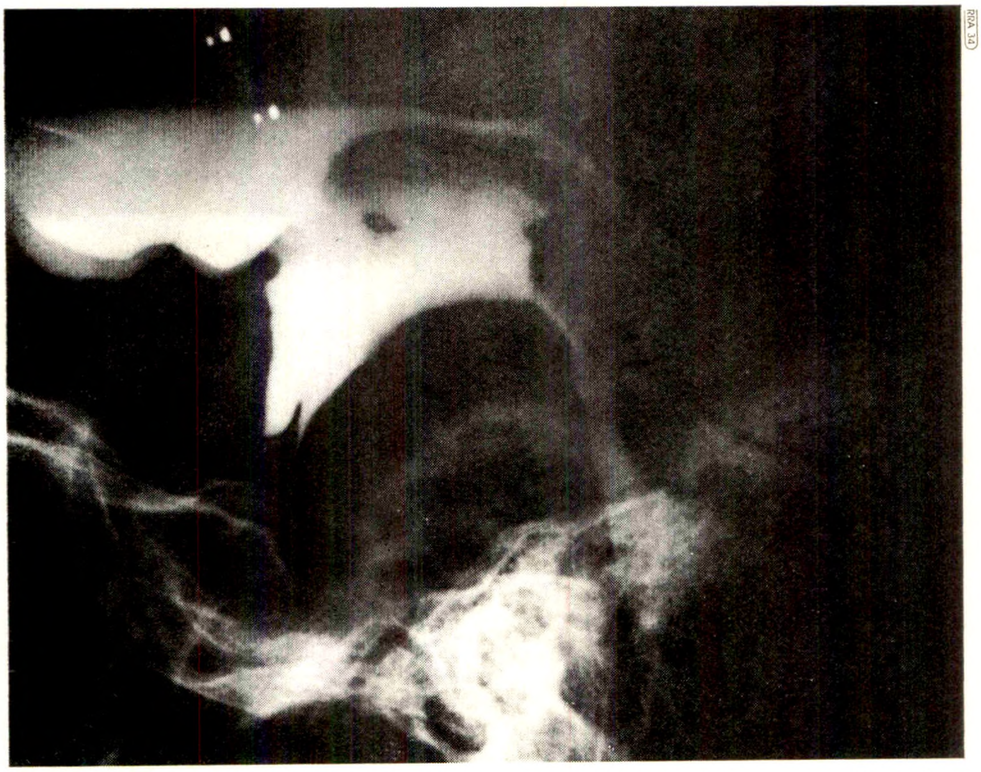

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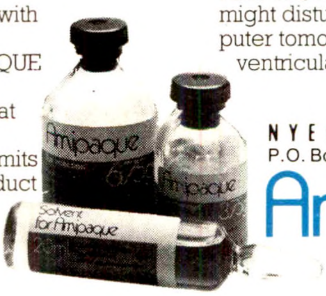

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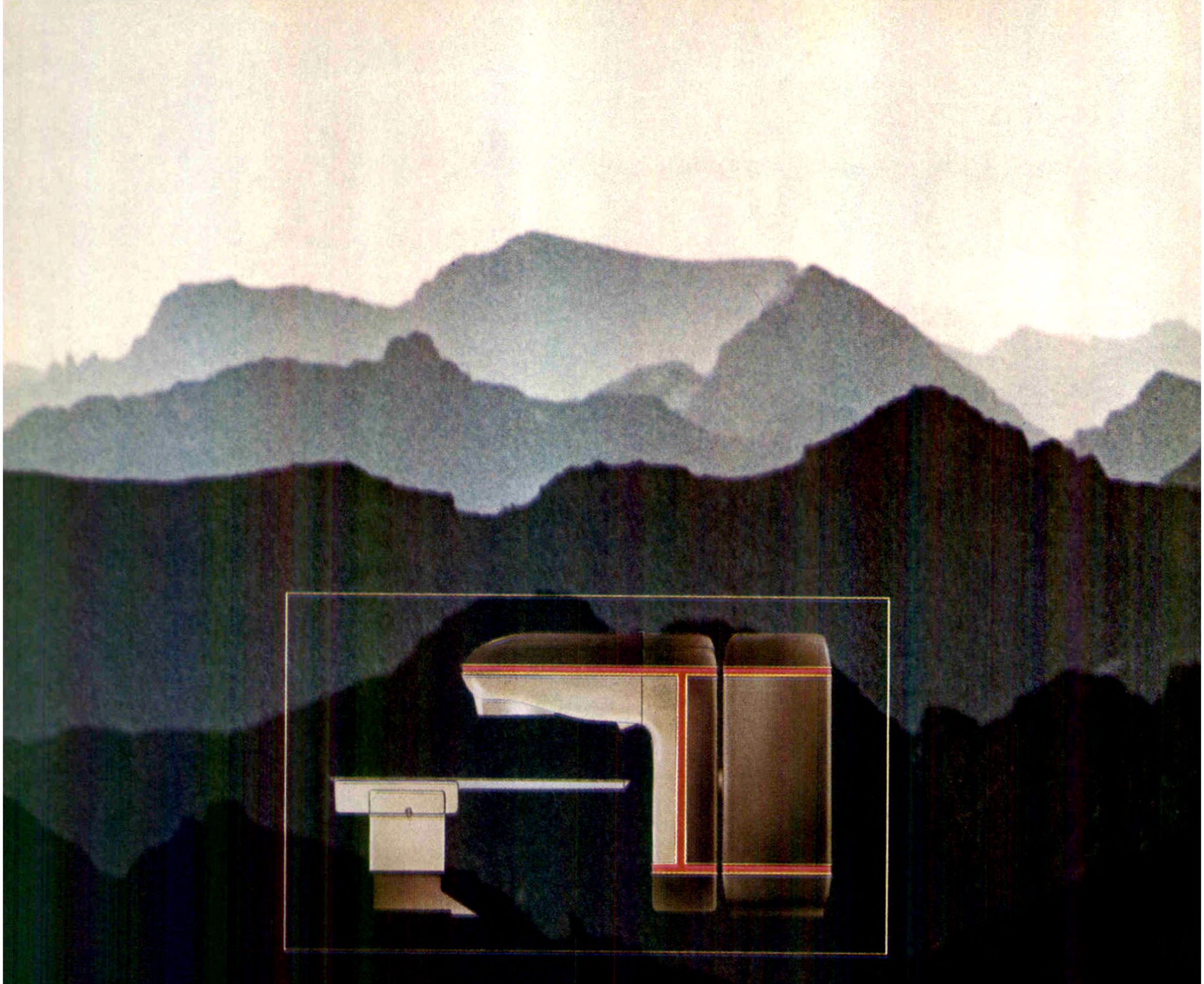

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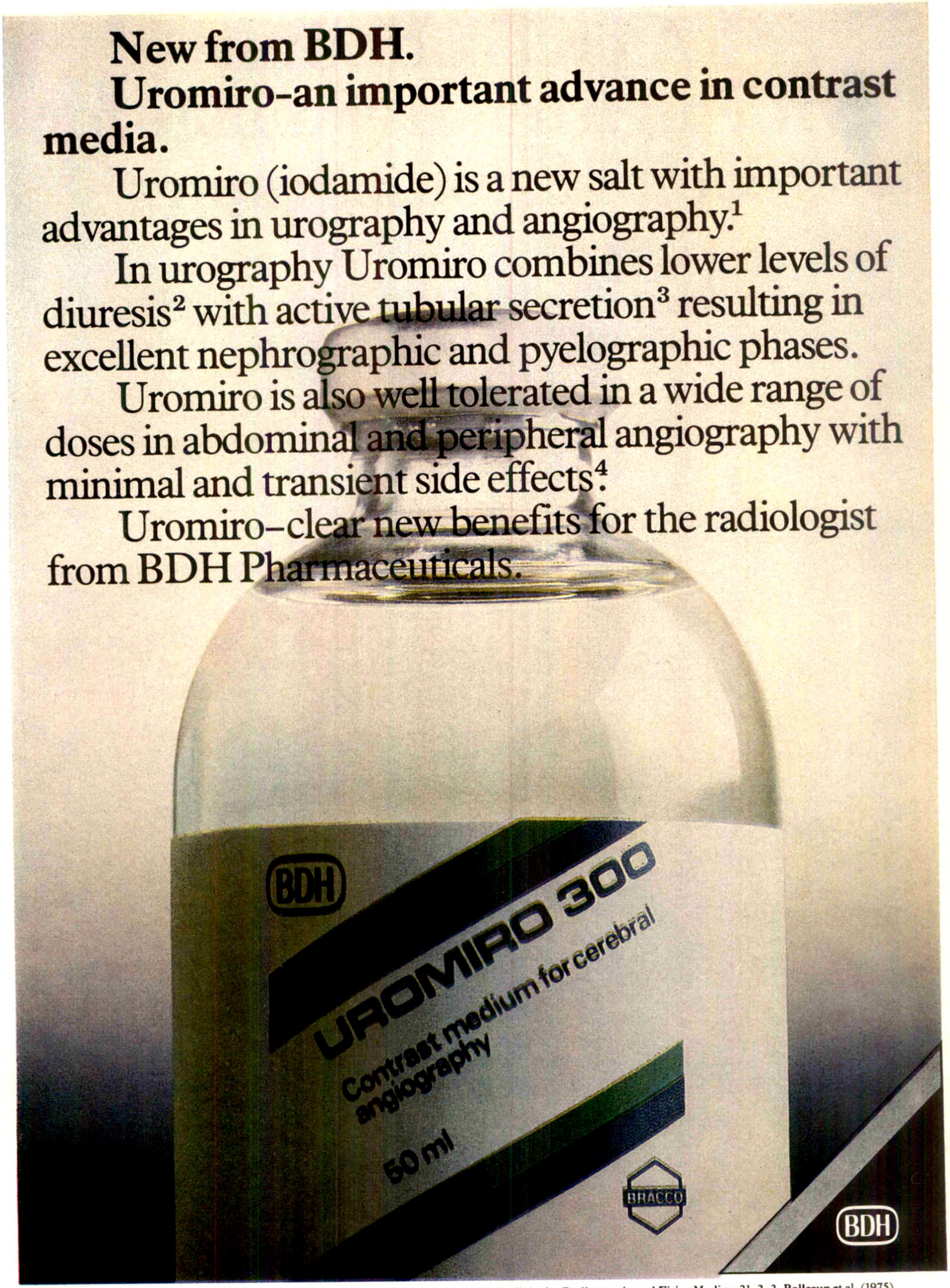

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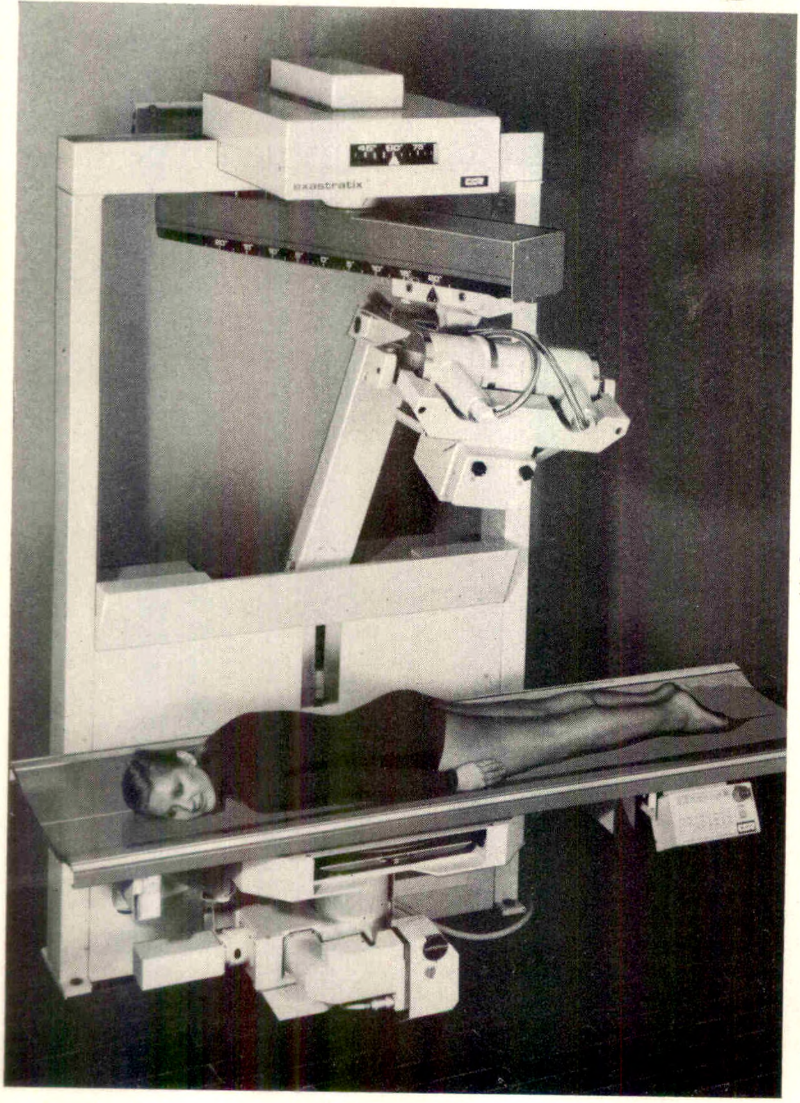

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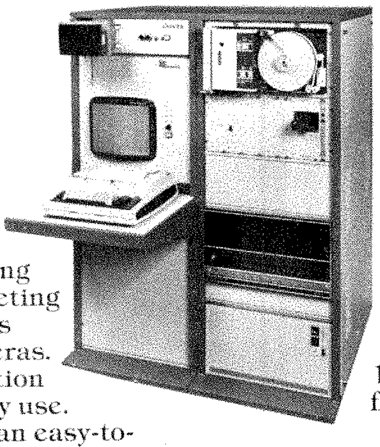

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The British Journal of Radiology (1975)

Supplement No. 13

The Pathogenesis of Reflux Nephropathy

(Chronic atrophic pyelonephritis)

By Professor C. J. Hodson, F.R.C.P., F.R.C.R., Memorial University of Newfoundland, Canada.
T. M. J. Maling, M.B., B.Ch., M.C.R.A., F.R.C.R. Christchurch General Hospital, New Zealand.
P. J. McManamon, M.B., B.Ch., L.G.M.C., F.R.C.R., General Hospital, Newfoundland, Canada, and
M. G. Lewis, M.B., B.S., M.D., M.R.C.Path, Cancer Research Unit, McGill University, Montreal.

The association between vesico-ureteric reflux and renal damage has been recognized for some time, but it has usually been assumed that the damage is due to infection promoted by the reflux. However, observations by Rolleston and his colleagues in New Zealand have indicated a link between the severity of reflux and renal damage.

Furthermore they have suggested that reflux penetrating into the renal substance is the factor most likely to explain the production of renal scarring.

These observations have been given a firm experimental basis by Professor Hodson and his associates. Their careful work on the growing pig has shown that the sites of intra-parenchymal or intra-renal reflux (IRR) are the sites of subsequent scarring and atrophy. IRR only occurs above a critical pressure level; reflux at lower-pressures produces no evident damage. Infection aggravates scarring but, in the presence of IRR, scarring can occur with sterile urine.

The work set out in this monograph has wide practical implications, and is of interest to paediatricians, nephrologists, urologists, radiologists and others concerned in the management of patients with urinary tract infection.

PRICE: £1·90 (Members of The British Institute of Radiology £1·75)

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The British Journal of Radiology (1978)

Supplement No. 14

Reflux and Renal Scarring

by P. G. Ransley, M.A., M.B., F.R.C.S. and R. A. Risdon, M.D., M.R.C.Path. of the Departments of Paediatric Surgery and Histopathology, Institute of Child Health, Guildford Street, London WC1.

Professor C. J. Hodson and his colleagues have shown the essential link in the association of chronic pyelonephritis with vesico-ureteric reflux: renal scarring in the growing kidney is related to intrarenal reflux of urine ("The Pathogenesis of Reflux Nephropathy", British Journal of Radiology Supplement No. 13, 1975). These ideas have now been taken further by Ransley and Risdon, again using the growing kidney of the infant pig. Their starting point is the morphology of the renal papilla. The different shapes of papillae, determined by the lobar structure of the kidney, are critical to the occurrence of intrarenal reflux.

These meticulous experimental studies answer many of the questions which have beset this subject: what are the pressure relationships of intrarenal reflux, why does scarring occur at predictable sites within the kidney, what are the mechanisms of progressive pyelonephritic deformity?

The authors have carried out carefully controlled experiments to test the importance of infection to renal scarring. Does sterile intrarenal reflux alone lead to scarring? Ransley and Risdon show that infection is an essential component to the initiation of the renal scar.

This work has far-reaching practical implications for understanding chronic pyelonephritis, and therefore for its medical/surgical management. Paediatricians, nephrologists, urologists, radiologists and all who care for children with urinary infection will read it with interest.

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1979, *British Journal of Radiology*, *52*, 1
VOLUME 52 NUMBER 613 JANUARY 1979

The British Journal of Radiology

Editorial

Use of SI units of radiation in the Journal

The new units for radiation have been gradually approaching for some time. The last editorial on the subject was in October 1972 (*British Journal of Radiology*, *45*, 715) and invited comment and discussion but no date was given when the new units would be introduced.

An article in the *BIR Bulletin* (Vol. 2, January 1976, page 6) explained the new units succinctly. The British Committee on Radiation Units and Measurements (BCRU) has now issued its recommendations on the introduction of the new units (published by NPL, May 1978). BCRU recommends that during an interim period both units should be used in official documents, the new unit to be given first, followed by the old unit in parentheses. BCRU further recommends that the old units should be abandoned for official use at some time during the period 1982–1985.

We do not yet know what attitude H.M. government will take to these recommendations, but THE BRITISH JOURNAL OF RADIOLOGY must decide when the interim period is to begin for papers in this journal. Already we have published several papers in which absorbed dose has been given in Gy, and many radiotherapy departments are actively considering the changeover.

The Editorial Committee has decided that the interim period cannot start before Volume 53, January 1980. Accordingly the new Instructions to Authors, appearing in this number of the Journal, requests that all new papers to appear in Volume 53 onwards should use the new unit first, with the old one in parenthesis. The date when the old units will be abandoned has not yet been decided.

The new units are becquerel (Bq), gray (Gy) and sievert (Sv). There is no specific unit for exposure which can only be expressed in coulomb per kg; the röntgen will disappear. Measurements in X-ray beams can be expressed as kerma, Kinetic Energy Released per unit MAss. One röntgen of X rays gives a kerma of 8.7 mGy (0.87 rad) to air. It is normally more useful to express a quantity of X rays in terms of tissue kerma, this being the dose received by a small volume of tissue at the point of interest. Multiples and sub-multiples of units will normally be in factors of 10^3 but the centigray (cGy) will be permitted for radiotherapy; use of the centigray is under active discussion in our correspondence column. The cSv will not be permissible.

There is no point in insisting on SI in the radiation field unless we do the same throughout. Thus concentration will have to be molar when the chemical formula is known. Some non-SI units will still be acceptable, for example minute, hour, litre and minute of angle. As far as we know, mm Hg for blood pressure and mm H_2O for other body pressures, barn for nuclear cross-sections, and eV for particle energy will remain acceptable for an indefinite period.

A conversion table between Ci and Bq is added here for the convenience of readers.

CONVERSION TABLE

Ci	Bq	Bq	Ci
1 nCi	37 Bq	1 Bq	27 pCi
1 μCi	37 kBq	10 Bq	270 pCi
10μ Ci	370 kBq	100 Bq	2.7 nCi
30 μCi	1.11 Mbq	1 kBq	27 nCi
100 μCi	3.7 Mbq	10 kBq	270 nCi
1 mCi	37 Mbq	100 kBq	2.7 μCi
10 mCi	370 Mbq	1 MBq	27 μCi
100 mCi	3.7 GBq	10 MBq	270 μCi
1 Ci	37 GBq	100 MBq	2.7 mCi
10 Ci	370 GBq	1 GBq	27 mCi
100 Ci	3.7 TBq	1 TBq	27 Ci
1 kCi	37 TBq	1 PBq	27 kCi
1 MCi	37 PBq	100 PBq	2.7 MCi
30 MCi	1.11 EBq	1 EBq	27 MCi

The number of significant figures should be appropriate to the precision required. 1 Bq is actually 27.027 pCi.

D. K. BEWLEY, F. STARER

1979, *British Journal of Radiology*, *52*, 2–13

Nuclear power and the environment

The Sylvanus Thompson Memorial Lecture delivered at the British Institute of Radiology joint meeting and annual congress on Friday, April 14, 1978

By Sir John Hill

United Kingdom Atomic Energy Authority, 11 Charles II Street, London SW1Y 4QP

(*Received April, 1978*)

There are so many aspects of nuclear power and the environment that it would be possible to give several quite different lectures all equally relevant to the title. There are, however, two quite separate aspects of the problem which are currently in the public eye and I would like today to concentrate on them. The first is the problem of the harmful effects of low levels of radiation which inevitably accompany any nuclear power programme and the other is the problem of radioactive waste management and the ultimate disposal of long-lived fission products.

Let me deal first with the low levels of radiation which accompany a nuclear power programme, and for that matter the whole radiological industry whether associated with hospital diagnosis, industrial X-ray examination or, for that matter, passenger baggage examination at our airports.

NATURAL BACKGROUND RADIATION

Table I shows the *per caput* radiation dose per annum received by the population of this country at the present time. It will be seen that natural radiation is far and away the principal source of this radiation. Some of this natural radiation comes from outer space, but the majority is from naturally occurring radioactive substances on the surface of the earth. This naturally-occurring radioactivity is dying away slowly with time and must have been considerably higher at the time when life was first evolving on this planet. The principal source of naturally-occurring radioactivity is now uranium 238 and its daughter products. ^{238}U has a half-life of 4 500 million years, almost exactly the same as the life of the earth itself. By this I mean that the radioactivity associated with ^{238}U has now fallen to half the level it was when the earth was created 4 500 million years ago.

TABLE I

ANNUAL DOSE TO GONADS IN UK FROM ENVIRONMENTAL RADIATION

Source	mrem	%
Natural background	96	74
Medical irradiation	~30*	23
Fallout	2	1.5
Nuclear wastes	0.2	0.2
Occupational	0.7	0.5
Luminous watches	0.2	0.2
Air travel	0.6	0.5

*UKAEA estimate.

Figures taken from private communication NRPB/UKAEA, 4th April 1978.

Since radiation is harmful, it can be argued that it is unfortunate that God left uranium distributed throughout the earth's crust. However, this uranium also has beneficial effects. The radioactivity associated with ^{238}U is the principal source of heat in the depths of the earth and provides the energy for the building of mountains and the movement of continents. Without this continuous mountain building and earth movement the land masses would long ago have been eroded away by water and it is most unlikely that mankind could ever have evolved at all.

The level of natural radioactivity is not, of course, the same everywhere since it is largely dependent upon the nature of the rocks and the quantity of radioactive materials (essentially uranium and thorium) contained in them. In this country the granite rocks of the north and west contain significantly more uranium than the younger sedimentary rocks in the south-east and this results in differences in the total levels of naturally-occurring radioactivity; for example:

London — 67 mrem per annum
Aberdeen — 106 mrem per annum

These differences in radiation levels are substantially influenced by the materials from which houses are constructed. Houses reduce the amount of radiation coming from outside, but can increase the level of radiation to the occupants by virtue of their own contained radioactivity. In a brick house in London the level of terrestrial radiation can be as low as 30 mrem per annum, while in an Aberdeen house built of granite the terrestrial radiation level can be as high as 150 mrem per annum.

But these changes are small by comparison with variations in radioactive levels in other parts of the world. If we ignore uranium mines and consider simply the activity levels on the ground we find that the highest radiation levels are usually associated with thorium deposits. Some of these deposits are very rich in thorium, approximately 10% by weight. In India the thorium sands along the Kerala coast extend for about 55 kilometres and about 70 000 inhabitants live there in radiation fields of up to 2 000 mrem per annum, *i.e.* 20 times higher than in London. In Brazil some of the coastal resorts near Rio de Janeiro are built on similar thorium deposits and thousands of holiday makers flood annually to towns such as Guarapari which have similar radiation levels.

Potassium is another naturally-occurring radioactive material which contributes significantly to the dose rate received by the human body. The isotope ^{40}K has a half-life of 1 260 million years. It is important because it is an essential constituent of the body and contributes about 20 mrem per annum from internal radiation. Incidentally a sleeping partner increases this radiation by about 1 mrem per annum.

Cosmic rays from outer space also contribute to naturally-occurring radiation. The earth's atmosphere is, however, a very effective shield and reduces the level of radiation to about 28 mrem per annum at sea level. At high altitudes, however, the screening effect is, of course, reduced and at 2 500 metres (about the height of Mexico City) the cosmic ray contribution is about double that at sea level. Flying in jet aircraft also increases radiation uptake. A long haul aircraft journey, say to the West Coast of the United States, will result in increased radiation of about 3 mrem.

My object of discussing naturally-occurring radiation at the start of this talk is not to attempt to prove that radiation is good for you, but to emphasize:

1. That radiation has always been present on the earth and that the levels have been higher in the past than they are today.
2. That there are very significant differences in the radiation levels at different places.

MAN-MADE ENVIRONMENTAL RADIATION

I would like now to turn to man-made radiation because this has become significant only recently since X rays and radioactive materials have been exploited for man's use. In the UK (and in all other developed countries) the principal source of radiation after natural radiation results from medical diagnosis. In this country this amounts to about 30 mrem per annum *per caput*. The average *per caput* radiation resulting from X-ray diagnosis differs markedly from country to country. In the less developed countries the figures are very low simply by virtue of lack of medical facilities.

The highest radiation levels from this source are given in the United States, Sweden and Japan, and it is generally true that in spite of rapidly improving techniques radiation levels for X-ray diagnosis are increasing as more examinations are made (U.N., 1977). Japan has a quite unusual characteristic in that while the radiation levels resulting from the examination of the extremities are very similar to those here, the major source of radiation in that country comes from X-ray examination of the stomach and upper intestinal tract. This tendency is also noticeable in the United States, although not to the same extent as in Japan. The radiation levels received from diagnostic X rays in Japan, Sweden and the United States are about three times higher than in the United Kingdom and are about the same as the natural background radiation in those countries. In other words, the medical profession has in those countries doubled the average radiation level as far as humans are concerned.

After God and the medical profession the next largest source of radiation is the military. The first weapons tests carried out in the atmosphere with weapons of about 20 000 tons TNT equivalent contributed just over 1 kg of fission products and a few kilograms of plutonium to the atmosphere. This activity soon spread right round the northern hemisphere and could readily be detected as fall-out or in rainfall. The activity increased steadily with the size and number of weapons to be tested until finally, in 1962, a number of vast weapons were detonated by the Americans in the Pacific and by the Russians in the Arctic. These detonations of 1962 had a total yield of 217 megatons of TNT and a fission yield of 76 megatons. They released more activity to the world than all the other tests put together and, of course, vastly more than any peaceful nuclear programme. These explosions caused an immediate and significant increase in world radiation levels. Justifiable and profound concern was expressed by all thinking people about the resulting pollution of our planet.

But with the banning of atmospheric tests (except by the Chinese) the atmosphere has now almost cleansed itself again and levels of activity have returned much nearer to pre-test values. This cleaning up process is, of course, a combination of two processes—fall-out, which is the process most important in the case of long-lived activity, and decay which is the dominant process for material of half-life less than about one year.

The dose commitment to the world's population due to these tests has however been high, perhaps 150 mrem to the population in the northern hemisphere and 100 mrem to the world's population as a whole—a cumulative dose of perhaps 300 000 000 man rem or one year's contribution from natural radiation.

Of the other sources of radiation only three are of significance—nuclear power, industrial X-raying and luminous watches. I am not being completely facetious in comparing nuclear power with luminous watches. Nuclear power does contribute a greater radiation to the population at large than luminous watches, but they are of the same order. Wrist watches are estimated to contribute a total of about 10 000 man rem per annum in this country. The new reprocessing plant at Windscale about which there has been so much controversy is expected to discharge activity corresponding to a dose commitment of not more than 20 000 man rem per annum. About half this radiation will be due to the inert gas Krypton 85 and when we are able to develop equipment for removing krypton this figure should be reduced to about 10 000 man rem. This plant will be capable of processing spent fuels from nuclear power stations of power equivalent to the burning of 100 million tons of coal per annum.

ENVIRONMENTAL RADIATION FROM THE NUCLEAR INDUSTRY

To get a full picture of the total radiation resulting from the nuclear industry in this country we must, however, consider all stages. The processing, enrichment and fabrication of uranium into fuel elements contributes a negligible routine dose as far as the public is concerned. As far as the workforce is concerned the degree of protection provided is that appropriate to a chemical industry dealing with a toxic product and radiation levels have only been a problem during failure of plant or failure of operating procedures leading to leakage or dust.

In nuclear power stations the core of the reactor is intensely radioactive (see Fig. 1). This is, of course, where the fission takes place and is far and away the most active part of the whole nuclear industry. It is, however, not necessary to approach the core during operation and all movements of fuel or controls are carried out remotely. Furthermore the active nuclear fuel and all the fission products are clad in metal tubes and the release of activity from the fuel elements is therefore minimal (Figs. 2, 3 and 4). The discharge of activity from nuclear power stations to the environment is therefore small. It corresponds to the activity associated with corrosion products in the fuel element ponds, cooling air which has become slightly activated by neutrons escaping from the core, and small quantities of tritium and sulphur 35 which are produced by neutron capture by trace impurities of lithium and chlorine in the core graphite.

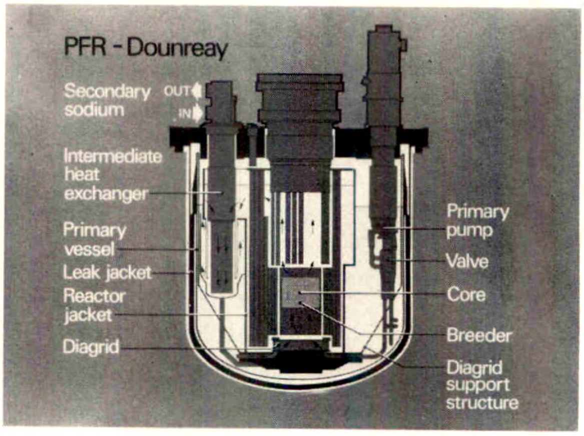

FIG. 1.
Simplified diagram of prototype fast reactor (PFR)
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The dose to the public from normal operation of nuclear power stations is therefore very small. It is in fact substantially less than from the fuel reprocessing plants. The total dose commitment to the British public from the British nuclear power programme is at present approximately 0.5 mrem per annum and this will be reduced substantially when new plant comes on stream at Windscale. This dose commitment is much smaller than the variations in natural radiation levels or variations in the average dose to the population at large resulting from changes in attitudes to medical diagnosis.

This is not to argue for lax rules in the nuclear industry. Under normal operating conditions the discharges to the environment are such that the irradiation levels to the public are very low indeed. But it must be remembered that nuclear power stations and reprocessing plants contain hundreds if not thousands of megacuries of activity and very stringent precautions are taken to ensure that these quantities of fission products are not, through accident, released to the environment.

It is perhaps at this point worth mentioning the rules which apply to radioactive wastes and emissions in this country. The standards are based upon

FIG. 2.
Assembly of experimental (PFR) breeder fuel at Reactor Fuel Laboratory, Springfields.
©*UK Atomic Energy Authority.*

recommendations of the International Commission on Radiological Protection (ICRP) that any unnecessary exposure to radiation should be avoided and all radiation doses should be kept as low as is reasonably achievable, economic and social considerations being taken into account. ICRP have recommended numerical dose limits designed to ensure that the risk to the health of individuals and populations should not exceed an acceptable level.

These guiding principles were embodied in United Kingdom policy and defined in a Government White Paper Command 884 (HMSO 1959) "The Control of Radioactive Wastes" as follows:

(i) To ensure, irrespective of cost, that no member of the public shall be exposed to a radiation dose exceeding the ICRP dose limit.

(ii) To ensure, irrespective of cost, that the whole population of the country shall not receive an average dose of more than 1 rem per person in 30 years.

(iii) To do what is reasonably practicable, having regard to cost, to reduce doses far below these levels.

These regulations are accepted by the nuclear industry as a fair interpretation of the ICRP recommendation and the nuclear industry works well within them. It is however interesting to note that the ICRP recommendation for the maximum dose to be received by any member of the public is 500 mrem per annum. Although these rules do not apply to natural radiation or radiation given for medical reasons, it is interesting to speculate how they would be interpreted if God had created the thorium sand deposits along the Sussex coast instead of along the coast of India and Brazil where they contribute up to 2000 mrem per annum.

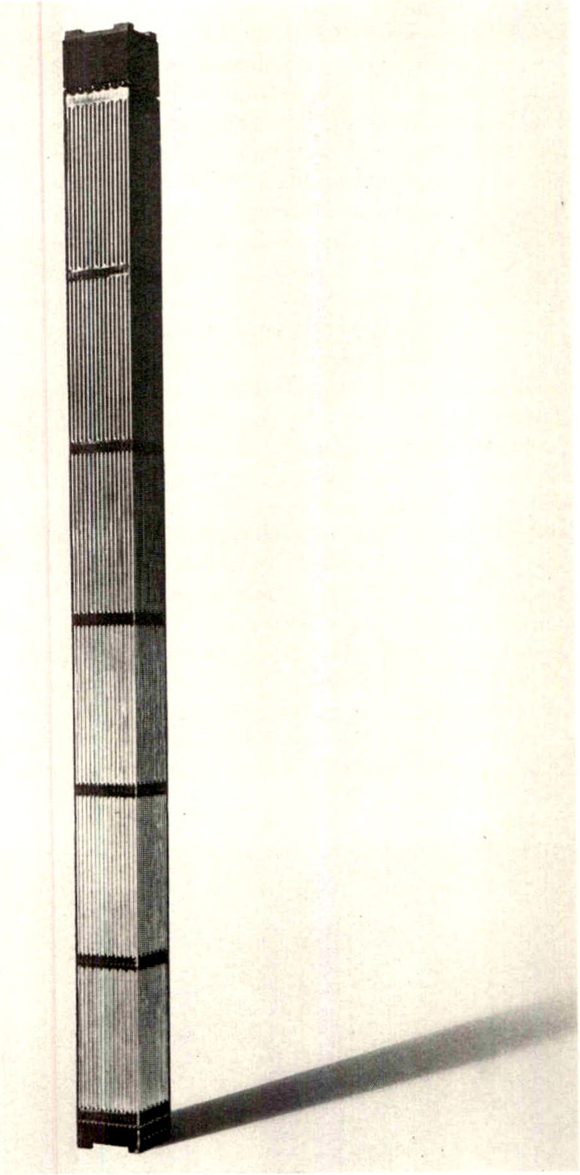

FIG. 3.
A Connecticut Yankee power water reactor (PWR) fuel assembly, Haddam Neck Plant.
©*Gulf General Atomic.*

There is no doubt that the nuclear industry operates under a particularly powerful microscope. In the foreword of the recent report by the Health and Safety Executive (HMSO 1978) on the hazards of conventional sources of energy it states:

"In all countries with a well developed nuclear industry the work started as a Government enterprise in which money and resources for health and safety studies, if not unlimited, were at least freely available. In addition, the consequences of ionising radiation were fairly well understood even 20 years ago and to this has been added the increasing experience available from such studies as those on the survivors of the weapons explosions at Hiroshima and Nagasaki. There is perhaps less understanding of the possible health effects of conventional energy sources largely because detailed studies have not been thought necessary.

"Against this background the process of health and safety assessment in the nuclear industry has developed along characteristic and possibly unique lines. In particular the level of protection achieved has been so high that there has been no real possibility of there being sufficient effects on the health either of the workforce or *a fortiori* of members of the general public to provide information on the consequences of the exposures to radiation and radioactive materials. Assessments of possible effects have therefore been based on a cautious extrapolation from levels of radiation dose known to produce effects in man down to those which actually occur in practice. In the case of members of the public this extrapolation involves factors in excess of a thousand. These very small exposures are indeed much less than the variations in the natural exposure to background radiation.

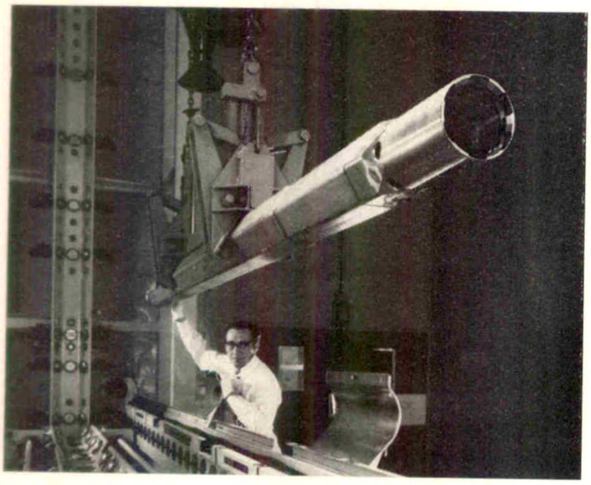

FIG. 4.

Transferring a completed PFR fuel sub-assembly to the vertical chamber gauge for final inspection. Fuel for the prototype fast reactor at Dounreay in Scotland is made at Windscale, Cumbria. It comprises mixed plutonium and uranium oxide pellets in stainless steel cans. The process plant is extensively automated and remotely controlled, particularly in the ceramic stages. The first charge, consisting of 32000 cans in 100 fuel sub-assemblies, has been completed and reload fuel is currently being manufactured. ©*UK Atomic Energy Authority*.

"It has been conventional to assume that these very small doses may produce deleterious consequences if the number of people exposed are large enough even though the risk to the individual is genuinely trivial and certainly never going to be demonstrable. By contrast almost all work on conventional pollution such as that arising from conventional sources of energy has been concerned with demonstrating whether or not observable effects are detectable at levels currently found in the environment or occasionally extrapolating downwards by one, or at the most two, orders of magnitude from levels which are known to produce observable effects in man. Unless agreement can be reached on a consistent approach, comparisons of the assessment of health and safety effects between nuclear and other sources of energy will always be unrealistic."

HAZARD FROM SMALL DOSES OF RADIATION

The information that we have on damage or injury by radiation is mostly derived from observable effects of high levels of radiation which resulted in the early days from the use of luminizing paint and more recently from the effect of X-ray therapy, the history of survivors of Hiroshima and Nagasaki and the effects of large doses of radiation received by workers involved in nuclear accidents.

From these large doses it is possible to deduce some correlation between the dose received and the increased probability of a cancer starting in subsequent years. This probability is approximately 10^{-4} per man rem. By this it is meant that a dose of shall we say 100 rem would result in an increased probability of cancer of 1% in subsequent years. What is not clear is whether this correlation is linear; does, for example, 1 rem give an increased probability of 10^{-4} of a cancer being produced in subsequent years? So far it has not been possible to establish whether or not this extrapolation is accurate because any figure such as 10^{-4} is completely swamped by statistical variations of the population and other factors which can cause or prevent cancer.

While it must be accepted that all radiation—even at low levels—is damaging, we might nevertheless expect that low doses would be less damaging than a linear extrapolation would predict.

On the other hand there would appear to be an almost direct relationship between the amount of meat consumed and the incidence of cancer in the large intestine (Fig. 5). Other factors such as lack of adequate roughage in the diet may, of course, be just as important.

For the public at large the average radiation received from the nuclear industry is so low that there is clearly no possibility of deducing anything about the effects of low levels of radiation from general health and mortality statistics. For radiation workers however the exposure to radiation can be up to 50 times higher than the natural background and exposures of up to ten times the natural background are fairly common. Numerous statistical analyses have been carried out to try and ascertain whether these radiation levels can be shown to have any measurable effect on the health or longevity of radiation workers, and, in particular, whether the linear extrapolation hypothesis for carcinogenesis is valid.

Although from time to time workers in various parts of the world claim to have demonstrated that some particular cancer has a higher incidence than would be predicted by the linear damage hypothesis I have not yet seen any convincing analysis. It is, of course, even more difficult to prove from mortality statistics that low levels of radiation are less damaging than the linear hypothesis would predict.

In the recently published recommendations of the International Commission on Radiological Protection (1977) it states "There are radiobiological grounds for assuming that the dose response curve for low-LET radiation will generally increase in slope with increasing dose and dose rate . . ." and "For many effects studied experimentally, the response in this range [up to a few hundred rad] can be represented by an expression of the form $E=aD+bD^2$" and later "The use of linear extrapolations, from the frequency of effects observed at high doses, may suffice to assess an upper limit of risk, with which the benefit of practice, or the hazard of an alternative practice—not involving radiation exposure—may be compared. However, the more cautious such an assumption of linearity is, the more important it becomes to recognize that it may lead to an overestimate of the radiation risks, which in time could result in the choice of alternatives that are more hazardous than practices involving radiation exposures. Thus, in the choice of alternative practices, radiation risk estimates should be used only with great caution and with explicit recognition of the possibility that the actual risk at low doses may be lower than that implied by a deliberately cautious assumption of proportionality."

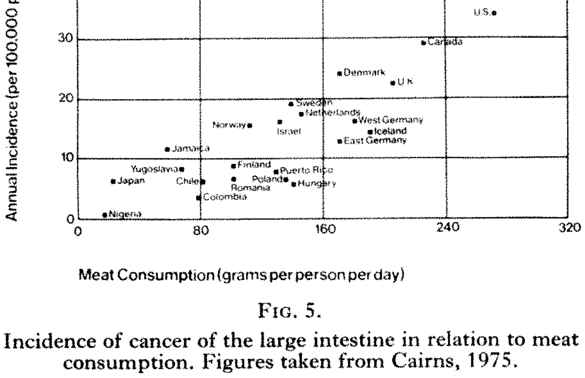

FIG. 5.

Incidence of cancer of the large intestine in relation to meat consumption. Figures taken from Cairns, 1975.

The linear hypothesis is of importance to the nuclear industry in two ways—to determine compensation payable to workers who have accumulated a significant radiation dose and die of a form of cancer, and as a basis for plant design.

A proportion of workers in any industry contract cancer, but in the case of radiation workers the linear damage theory can be used as an upper limit to establish the probability of the cancer being caused by radiation. Take for example a worker who has received a cumulative dose of 10 rem. Using the factor 10^{-4} we would calculate an excess probability of all forms of cancer of 10^{-3} in subsequent years. The probability of a man of say 35 dying of cancer of the lung over a 30-year period is however much higher, 3.5×10^{-2} over the period from 35 to 65.

But if we consider a very rare form of cancer—for example myeloma in young people—the probability of contracting this disease from natural causes is 6×10^{-5} between the ages of 25 and 44. If such a person had received the same integrated dose the linear hypothesis could set the upper limit of this being due to radiation which would be sufficiently high for compensation to be payable.

From the point of view of plant design, it is extremely important for the nuclear industry to know to what extent the linear hypothesis is valid, not of course to avoid paying compensation to unfortunate employees who die of rare forms of cancer but so that realistic estimates can be made of how much money should be spent to reduce radiation exposure not only to our employees but to the public.

Again referring to the Recommendations of the ICRP (1977), it says in paragraph 130 "In these recommendations, therefore, the Commission does not propose dose limits for populations. Instead it wishes to emphasize that each man-made contribution to population exposure has to be justified by its benefits . . ." "The limit for irradiation of a whole population is thus clearly seen as the total reached by a summation of minimum necessary contributions and not as a permissible total apparently available for apportionment."

In the nuclear industry hundreds of millions of pounds are being spent on establishments such as Windscale on the basis of a hypothesis which is assumed to be linear right down to the origin. Almost every other industry assumes that their damage curve has a cut-off point at some level, below which no damage occurs. This anomaly may well be leading to expenditure on nuclear plant to achieve minimum discharges to the environment, when the same money—and it is effectively all public money—could produce much greater benefits if applied to other pollutants.

I have discussed at some length the difficulty in obtaining information on radiation damage from the health and mortality statistics. It is not that there is any shortage of statistics, the real problem is that the variations in the statistics both for different occupations and different parts of the country are vast compared with anything that could be attributed to radiation.

I have below picked out from the latest mortality statistics published by the Office of Population Census and Surveys (HMSO 1974a) the standardized mortality rates for three common causes of death—cancer of the lung, cancer of the stomach and ischaemic heart disease. I have selected these particular causes of death because the numbers involved are large and therefore the statistical accuracy is much better than for rarer diseases. The figures given correspond to an average of 100 for the whole of England and Wales.

TABLE II

Variation by area of mortality from three common causes of death

	Cancer of lung	Cancer of stomach	Ischaemic heart disease
Northern	114	123	115
Yorkshire & Humberside	102	101	112
North West	110	117	111
East Midland	90	90	98
East Anglia	89	90	84
South East	103	89	91
South West	82	94	93

Figures taken from the Registrar General's Mortality Statistics by Area—England and Wales 1974.

We see even greater variation when we study the mortality statistics of different industries. Let me give a few examples, again using the figure of 100 as standard for England and Wales (HMSO 1974b).

The only conclusion I want to draw from these two tables is the fairly obvious one that you get higher mortality figures in industries that are harsh and dirty and the same is true of those parts of the country where living conditions tend to be harder. But there may well be other reasons related to water supply, eating habits, social habits and so on. But with such large variations in different regions and different occupations, is enough analysis being given to other pollutants or deficiencies that can influence the health and life expectancy of the population when compared with the microscope focused upon the effects of low level radiation?

It seems to me, after studying the statistics produced by the Registrar General, that if we want to improve the health and life expectancy of the population we should move in the direction of cleaner and more professional industry and away from the dirty, dusty industries which employ unskilled manual workers. It is in this context that we, the nuclear industry and you the radiological industry, make our contribution in spite of using radiation as one of our principal instruments.

Treatment and Storage of Fission Products

But we in the nuclear industry suffer a further disadvantage by comparison with the radiological industry. We have to deal with long life fission products whereas the radiographer can turn off the X-ray beam at the touch of a switch. I would like therefore to conclude by saying something of the treatment and storage of fission products in the nuclear industry.

Figure 6 shows the fission process and Fig. 7 the distribution of fission products from the burning of uranium. About 300 different nuclei have been detected and about 180 of them are radioactive.

TABLE III

Variation of mortality by occupation

Professional occupations	75
Farmers	91
Woodworkers	96
Electrical	104
Construction workers	111
Forge and foundry	122
Miners and quarrymen	144

Figures taken from the Registrar General's Occupational Mortality Statistics—England and Wales 1970–1972 Decennial Supplement.

These nuclei are unstable because the fission process produces the wrong balance of protons and neutrons in the nucleus; as this imbalance is corrected electrons and γ rays are emitted. A large number of these fission products have a very short half-life and die away to stable elements in seconds, minutes or hours; as far as radioactive waste is concerned they can be ignored because they will all have disappeared before the fuel is even withdrawn from the reactor.

Other fission products have half-lives of days or weeks and these can all be allowed to die away in the

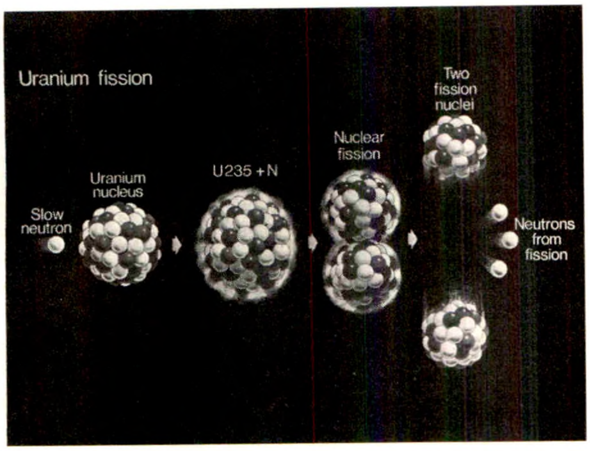

FIG. 6.

The fission process in a uranium nucleus. (From BNFL booklet "Working with Radiation").
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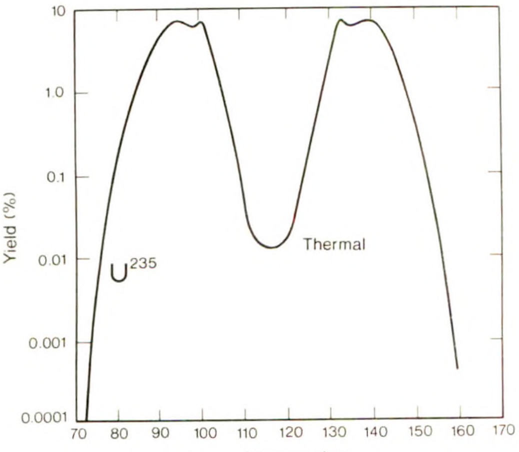

FIG. 7.

Distribution of fission products from the burning of uranium (Liverhant, 1960).
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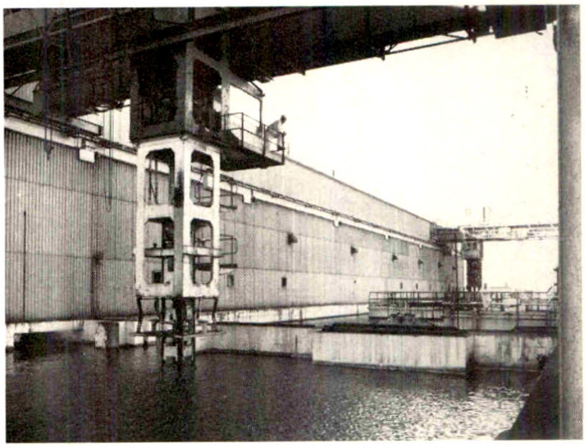

FIG. 8.

View of part of the cooling pond at Windscale works of British Nuclear Fuels Limited.
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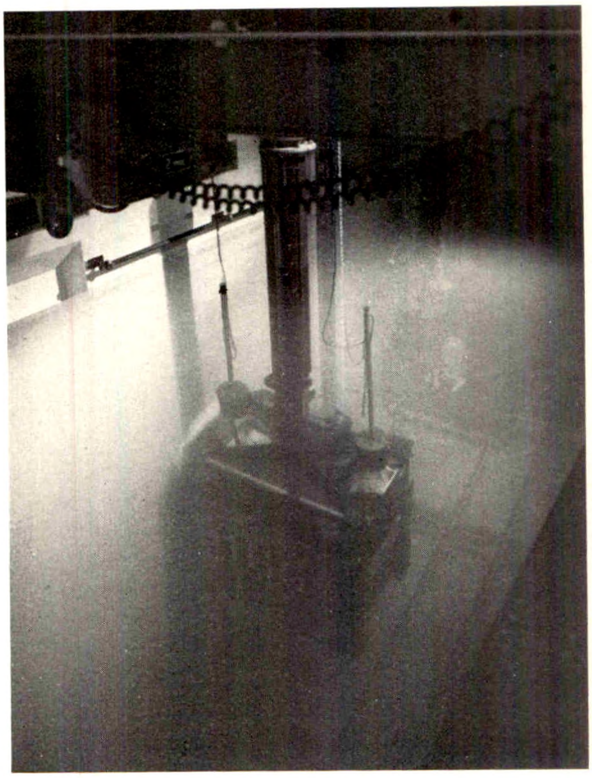

FIG. 9.

View of fuel flask in cooling pond. Each fuel element consists of 36 stainless steel fuel pins inside a graphite sleeve. The pins are filled with slightly enriched uranium dioxide pellets. When fully loaded each reactor contains 2464 fuel elements in 308 channels.
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cooling ponds before the fuel is processed (Figs. 8 and 9). A particularly important fission product in this class is iodine 131 with a half-life of eight days. In some ways this can be regarded as a particularly difficult fission product because it is very active, it is volatile, and it is readily absorbed in the body. On the other hand the fuel can be left in the cooling ponds for six months before processing by which time the activity of ^{131}I will have decayed to less than one millionth of what it was.

As we go up the scale in lifetime we come to those fission products with half-lives in months or years and these are the most important from a reprocessing point of view. Cerium 144 with a half-life of 284 days contributes the most activity in fuel about a year old. Ruthenium 103 with a 40 day half-life and ruthenium 106 with a half-life of exactly a year are particularly troublesome to process. Ruthenium is an element with many possible valencies; whatever you do to effect a separation some of it always turns up in effluent streams one would like to discharge.

The most difficult fission products are, however, strontium 90 and particularly caesium 137. These are both abundant with yields of about 5% of the total yield of fission products and have half-lives of about 30 years. This is short enough for them to be very active and yet it is too long to enable one to wait for them to decay away. They constitute the principal activity in nuclear waste over the period ten years old to 500 years old.

Finally, there are a very few fission products with half-lives of 10 000 or even 1 000 000 years but these are present in very small quantities and have such a low specific activity that they are of little consequence and contribute less activity than was possessed by the uranium that was dug out of the ground in the first instance.

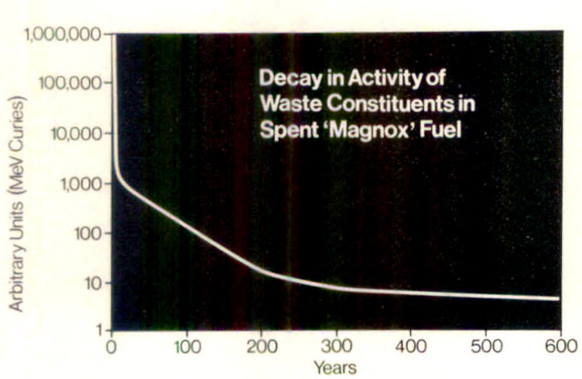

FIG. 10.

Decay in activity of waste constituents in spent "Magnox" fuel.
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Figure 10 shows how the activity of fission products decays with time. The important things to note are first the very rapid fall in activity in the first months or years after removal from the reactor. Second the steady slow fall in activity demonstrated by the 30 year halving time of ^{137}Cs and ^{90}Sr and finally the very small residual activity of the weak long-lived products.

The fission products, after separation from the plutonium and uranium, emerge from the reprocessing plant as a solution in nitric acid. It is at present concentrated as far as possible without causing crystallization or precipitation and is stored in high integrity tanks within thick-walled concrete vaults which are themselves clad in stainless steel (Fig. 11). Internal cooling coils are provided to remove fission product heat (Fig. 12) and the tanks also have an external cooling jacket which effectively provides an additional cladding. Spare tanks are always available together with means of transferring liquors from one tank to another if a leak develops.

Although the storage of these highly active wastes has been entirely satisfactory to date it is clear that we can do better than just leave them in an ever growing tank farm. Solidified waste is clearly much less likely to leak into the environment

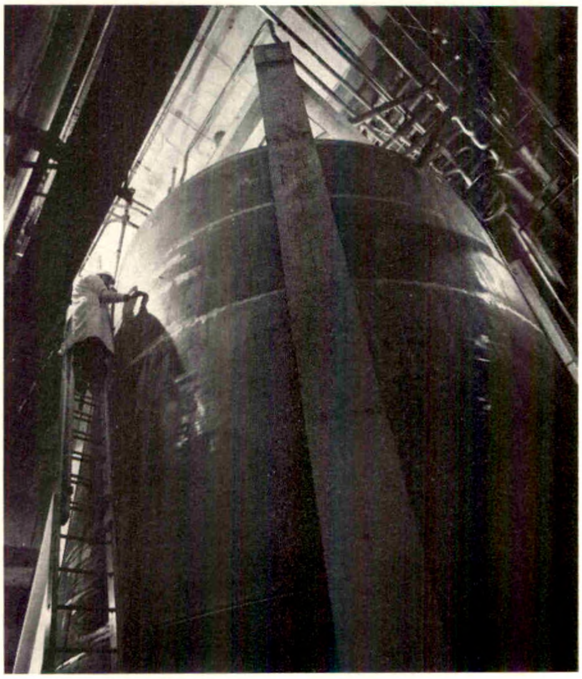

FIG. 11.

General view of highly active storage tank (Windscale).
©*British Nuclear Fuels Ltd.*

than a liquid and will require less supervision. It is therefore planned to glassify these wastes by mixing them with a slurry of the raw materials of glass and then raising the temperature to about 1000°C by which time all the volatiles will have boiled away and glassification will take place (Fig. 13).

This process was developed at Harwell over ten years ago. The fundamental process is no different from that which has been used in glassmaking for the last 2000 years and the main problem is how to engineer a plant to do this simple operation reliably and remotely with such highly active materials. There can be no possible doubt that it can be done on a full production scale. The only question is what is the best way from the point of view of cost, ease of operation and maintenance.

Prototype plants are now under construction and in about eight years' time we shall have a first production plant in operation. These plants will produce glassified waste in stainless steel cylinders, each cylinder containing about one ton of glass which, in turn will contain about one-fifth of a ton of fission products. Our nuclear programme is now equivalent to about 15 million tons of coal per year and produces about five tons of fission products which when glassified will amount to 25 cylinders of waste a year. The heat output will depend upon the age of the waste, but will be of the order of 10 kW per cylinder. The cylinders will be stored in deep ponds of water for another 20 to 30 years (see Fig. 14) until the heat output has diminished sufficiently for the next stage of disposal.

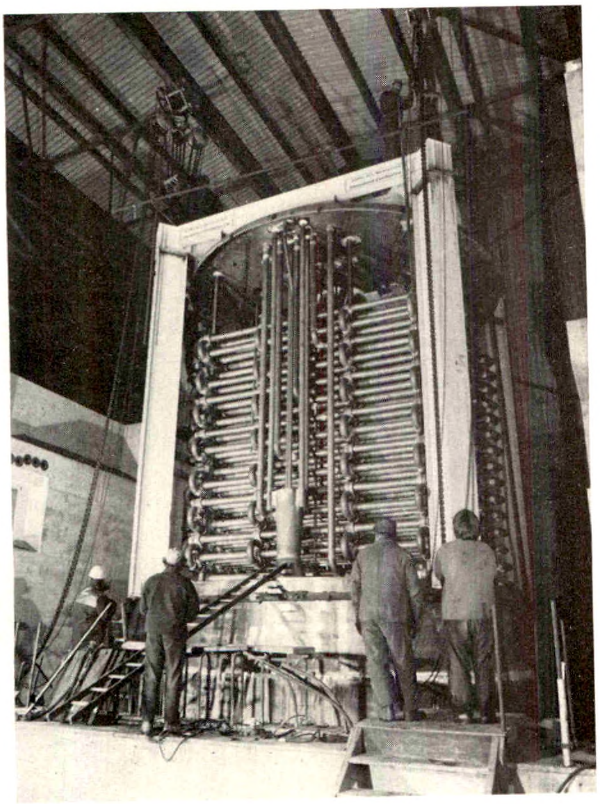

FIG. 12.

Lowering cooling coils into high activity storage tanks.
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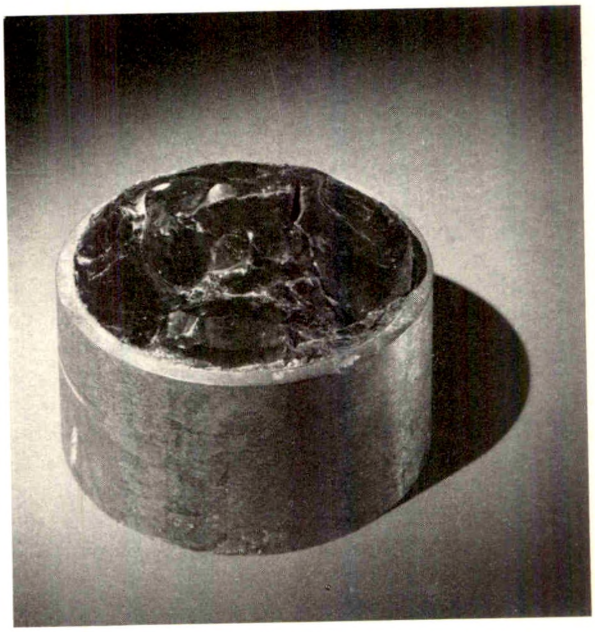

FIG. 13.

Section of a vessel containing vitrified waste with simulated fission products.
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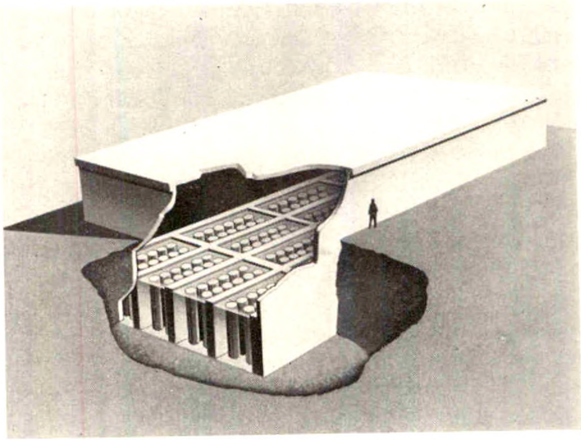

FIG. 14.

Diagram showing glass blocks stored under water.
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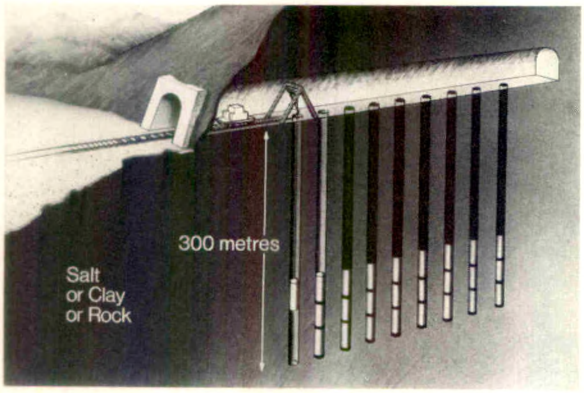

FIG. 15.
Diagram showing a possible way of disposing of highly active waste by burial in deep stable geological formations.
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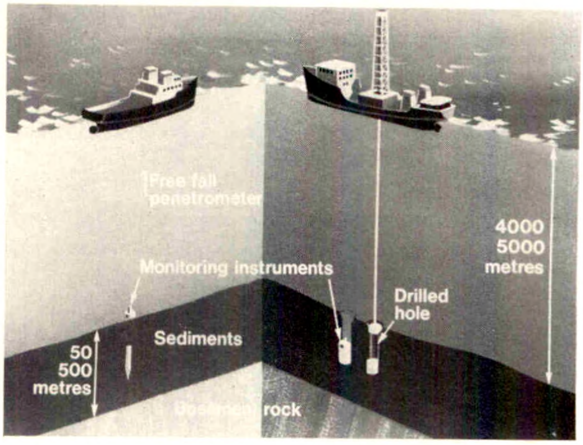

FIG. 16.
Diagram showing a possible way of disposing of highly active waste by burial at the bottom of the ocean.
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These cylinders have to be kept away from man for about 500 years until all the ^{137}Cs has decayed. We are therefore planning to bury them sufficiently deep in rock that people will not accidentally dig them up again without knowing what it is they have unearthed (see Fig. 15).

I believe you could bury these glassified wastes pretty well anywhere but because of the long time they have to be kept away from man and the fact that we do not want to have to supervise them in the future, we have looked for geological formations which should be particularly suitable and require no long term supervision. For the UK granite structures would appear to be the most suitable because unfractured granite should be free from water and only percolating water could possibly transport activity back into the food chain and then back to humans. Clay and salt deposits are other possible formations which are being studied. Sediments under the sea are also a possibility (see Fig. 16).

There is not really any great hurry to find an ultimate disposal site. If we bury fission products when they are still relatively young we will have problems of heat dissipation because rock does not have a high thermal conductivity. We would prefer to wait until the heat output of the glass is down to a level which can easily be conducted away. If we do not we will have to have a ventilated store, or some other cooling arrangements, for an equivalent period of time. But there are pressures upon us to demonstrate the principle of ultimate storage and we would certainly like to get the research and proving work done without a rush and in good time.

CONCLUSION

I would not like to give the impression that there are no problems in the nuclear industry. No large industry would claim that it is free of all problems. The amount of radioactivity in the core of a large power reactor is of the order of a thousand million curies during operation. Very stringent precautions have to be taken to ensure that this activity cannot by accident be discharged to the environment. Even when the reactor is shut down the fission products in the fuel remain intensely active and all parts of the plant near the core become active and must be maintained remotely.

The reprocessing of nuclear fuel is similarly a difficult operation both because of the difficulty of maintenance of a highly active plant and because in relation to the throughput of the plants much tighter controls are imposed upon the discharge of radioactive effluents than upon the discharges of most other industries.

But provided plants are properly designed and operated to high standards, there is no reason why the nuclear industry cannot provide this country with all the power it requires. Moreover it can do this with less impact upon the environment than that of alternative energy sources and with radiation levels to the population so low that they will always be much less than the variations in the level of natural radiation.

ACKNOWLEDGMENT

Permission by the UKAEA and Companies to reproduce the illustrations, as detailed, is gratefully acknowledged.

REFERENCES

CAIRNS, J., 1975. The cancer problem. *Scientific American*, *233*,

H.M.S.O. 1974A. Office of Population Census and Surveys. Mortality statistics Area Series DH 5, No. 1.

H.M.S.O. 1974B. Office of Population Census and Surveys, Occupational mortality.

H.M.S.O. 1959. The control of radioactive wastes. H.M. Government Command 884.

H.M.S.O. 1978. Health and Safety Executive Report. The hazards of conventional sources of energy.

International Commission on Radiological Protection 1977. *Publication 26, Annals of the I.C.R.P.*, *1*, 3.

LIVERHANT, S. E., 1960. In *Nuclear Reactor Physics* (John Wiley).

H.M.S.O. 1970–72. Registrar General's decennial supplement for England and Wales. Series DS1.

U.N. 1977. *Sources and effects of ionizing radiation*. Scientific Committee on the effects of atomic radiation.

Book review

Emmett's Clinical Urography. An Atlas and Textbook of Roentgenologic Diagnosis. 4th Edition. By D. M. Witten, G. H. Myers and D. C. Utz, pp. xxii+2250+index, illus., 1977 (East Sussex, W. B. Saunders Co.), 3 volume set, £75·00.

The delight with which a new edition of this standard textbook of uroradiology is welcomed will be tempered by the knowledge of the death of its founder and driving force, Dr. John L. Emmett. The quality of this edition will serve as a fitting tribute to a great man to whom so much is owed by radiologists and urologists throughout the world. It is appropriate that this edition should be entitled "Emmett's Clinical Urography".

In addition to the three editors there are no less than 20 contributors each of whom has already justifiably earned a high reputation in the field of uroradiology. As before, the edition is presented in three volumes but now has 20 chapters and runs to no fewer than 2250 pages. Approximately two thirds of the edition comprises the atlas which is incorporated in suitable positions among the text. There are three new chapters; Renal mass puncture and percutaneous translumbar pyelography; Techniques and applications of sonography and computed tomography which represents a logical juxtaposition of these two techniques; Renal failure and renal parenchymal disease. The atlas constitutes arguably the best collection of illustrations of the normal and abnormal radiological appearances of the urinary tract available anywhere. Some of the newly included grey scale ultrasound illustrations and a few of the CT images are not up to the otherwise uniformly excellent standard. This must reflect the early stages of the development of these techniques and doubtless this minor shortfall will be corrected in future editions. The legends to all the illustrations are in themselves self-sufficient and allow for rapid reference to problems that present in day-to-day practice.

Virtually every condition is properly illustrated and the editors have not hesitated in requesting suitable examples from other experts. The text is presented in a logical order and successfully provides a basic reading for the beginner and a ready source of reference to the experienced practitioner. There are abundant well-selected references at the end of each chapter with, when relevant, additional suggestions for further reading and research. The text does tend to present as many problems as it solves but this reflects the intriguing character of the whole subject.

The editors are to be congratulated in maintaining the high standard of the previous editions and in appropriately reflecting the many and rapid advances in the subject. This edition should be present in all departments of radiology and available to all students of the subject.

JOHN ROYLANCE.

1979, *British Journal of Radiology*, *52*, 14–23

Bone densitometry using computed tomography

Part I: selective determination of trabecular bone density and other bone mineral parameters. Normal values in children and adults.*

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ABSTRACT

Gamma-ray computed tomography (γ-ray CT), using a special purpose scanner, enables *in-vivo* quantitative analysis of bone mineralization. Trabecular bone density (TBD), the relative amount of compact bone (bone density, BD) and the total absorption (TA) for a cross-section of the radius are determined from measurements of local linear absorption coefficients. A preliminary study of normal children ($n = 49$) and adults ($n = 34$) indicated that TBD is independent of age and sex in the age range 4 to 40 years. DB remains constant throughout childhood but increases after puberty in both women and men. TA is higher for adults than for children, and also higher for men than for women. A correlation between TA and parameters relating to body size indicates a relationship between body weight and bone mass.

The method of photon absorptiometry (Cameron and Sorenson, 1963) is widely used for *in vivo* assessment of the mineralization of long bones. However, the resolution and the sensitivity of this technique do not permit the measurement of small changes in mineralization which may possibly occur during a period of weeks or months. A new measurement technique having greatly improved resolution and sensitivity in the measurement of bone mass has recently been described (Ruegsegger *et al.*, 1974; Ruegsegger *et al.*, 1976). This technique is based on gamma-ray computed tomography (γ-ray CT) and it has been applied to measurements of bone mineral distribution in the radius of normal children and adults. The radius lends itself particularly well to γ-ray CT since it is easily accessible; also, the metaphyseal region contains much trabecular bone, whereas the diaphyseal portion is a relatively uniform shaft of compact bone. Though the mineral content of the radius does not necessarily reflect the mineral content of other parts of the skeleton, there is evidence in many metabolic bone diseases that similar changes take place at different sites of the skeleton. Quantitative comparisons of bone mineral content at different skeletal sites have been made, *e.g.* by Burckhardt (1954) who determined the specific weights of trabecular bone in vertebrae and in long bones; by Meema (1973) who correlated the cortical thickness of the radius with multiple spinal compressions, and by Cohn *et al.* (1973) who related mineral content of the radial bone to total-body calcium.

In the present report normal values for size and mineralization of the radius as obtained by γ-ray CT are presented.

The importance of the interrelation between trabecular bone density and relative amount of cortical bone will be discussed in relation to metabolic bone diseases in a subsequent publication (Part II).

MATERIALS AND METHODS

Instrumentation

The γ-ray CT instrumentation and the analytical image reconstruction procedures have been previously described (Ruegsegger *et al.*, 1974; Ruegsegger *et al.*, 1976; Elsasser, 1977). The distribution of local linear absorption coefficients in a cross-section of the radius is determined by ^{125}I γ-ray CT and is interpreted as being equivalent to the bone density distribution. Visual inspection of the cross-sectional image which is obtained for example by representing the density in terms of a gray scale, or colour-coding, yields no more than a qualitative impression of the density distribution. For a quantitative analysis of bone density one has to use the computed density values of each picture element (Fig. 1). However, in this analytical process the surrounding soft tissue is disregarded, and thus the mean value of the linear absorption coefficient for all picture elements within the cross-section of the radius is also the mean linear absorption coefficient of the total bone cross-section.

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* This work was presented, in part, at the Joint Meeting of the European Society for Paediatric Research, European Society for Paediatric Endocrinology, and Working Group for Mineral Metabolism, Rotterdam, Netherlands, June 1976 (abstract published in ***Paediatric Research***, Exner *et al.*, 1976) and at the 61st Annual Meeting of the Federation of American Societies for Experimental Biology, Chicago, Ill., April 1977 (abstract published in *Federation Proceedings*, Elsasser and Exner, 1977).

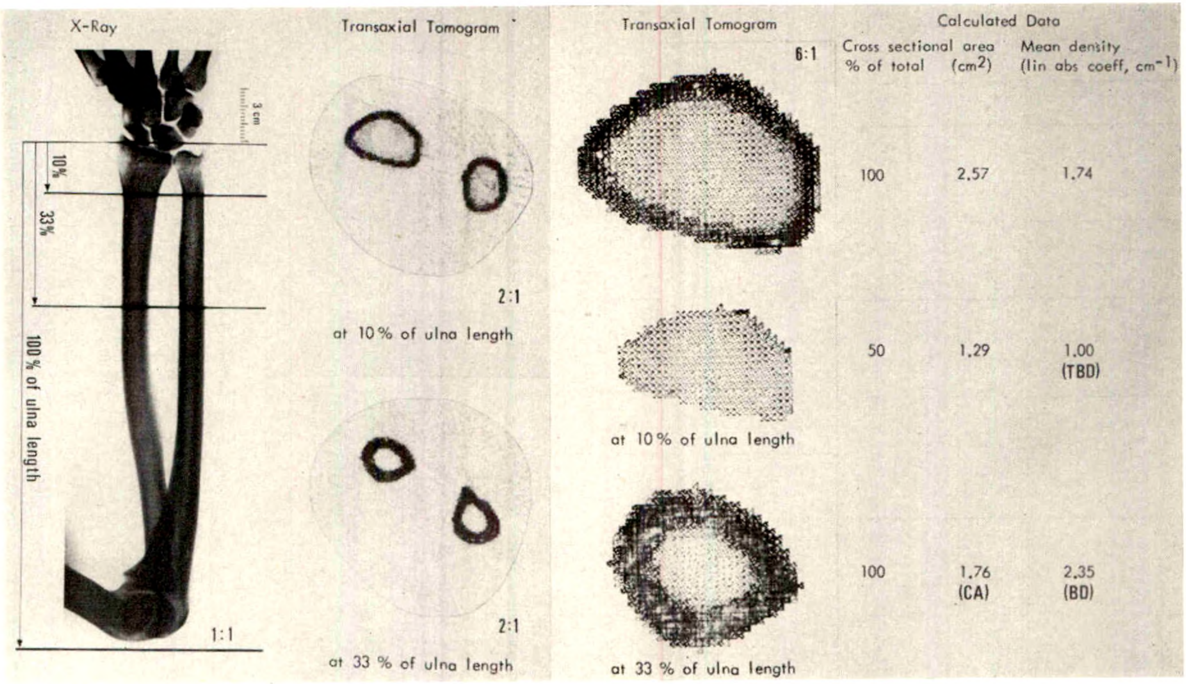

FIG. 1.

X ray with wires indicating the standard measuring sites and corresponding digital tomograms on the left. Evaluation of the cross-sections of the radius on the right. Normal man, 32 years old.

Concentric rings are then "peeled-off" the reconstructed bone image, and a mean linear absorption coefficient calculated for the remaining cross-sectional area. In this way it was found that a 50% "core" of the normal radius, at a site 10% of ulna length measured from the distal end, contains trabecular bone only. In contrast, at the 33% ulna length site the radius is essentially compact bone and marrow.

In a physical model simulating the distal region of the forearm the reproducibility in a measurement of the 50% core-value for a cross-section was better than ±1% (coefficient of variation (CV)=%SD) (Elsasser, 1977).

In this measurement procedure a 2 mm thick slice of the forearm is exposed to the ^{125}I γ rays during a period of 5 min. The radiation dose received by this part of the forearm has been calculated to be: 4.0 mrad for soft tissue: 2.3 mrad for bone, and 0.38 mrad for bone marrow.

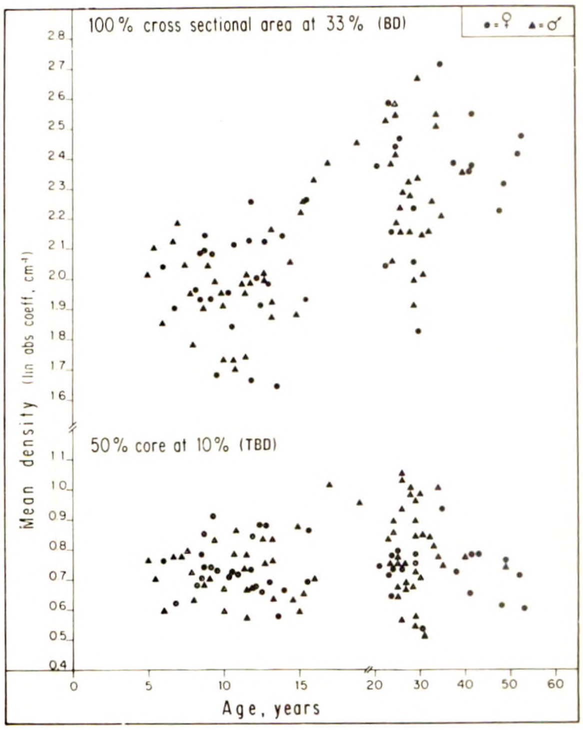

FIG. 2.

Distribution of TBD and BD according to age and sex.

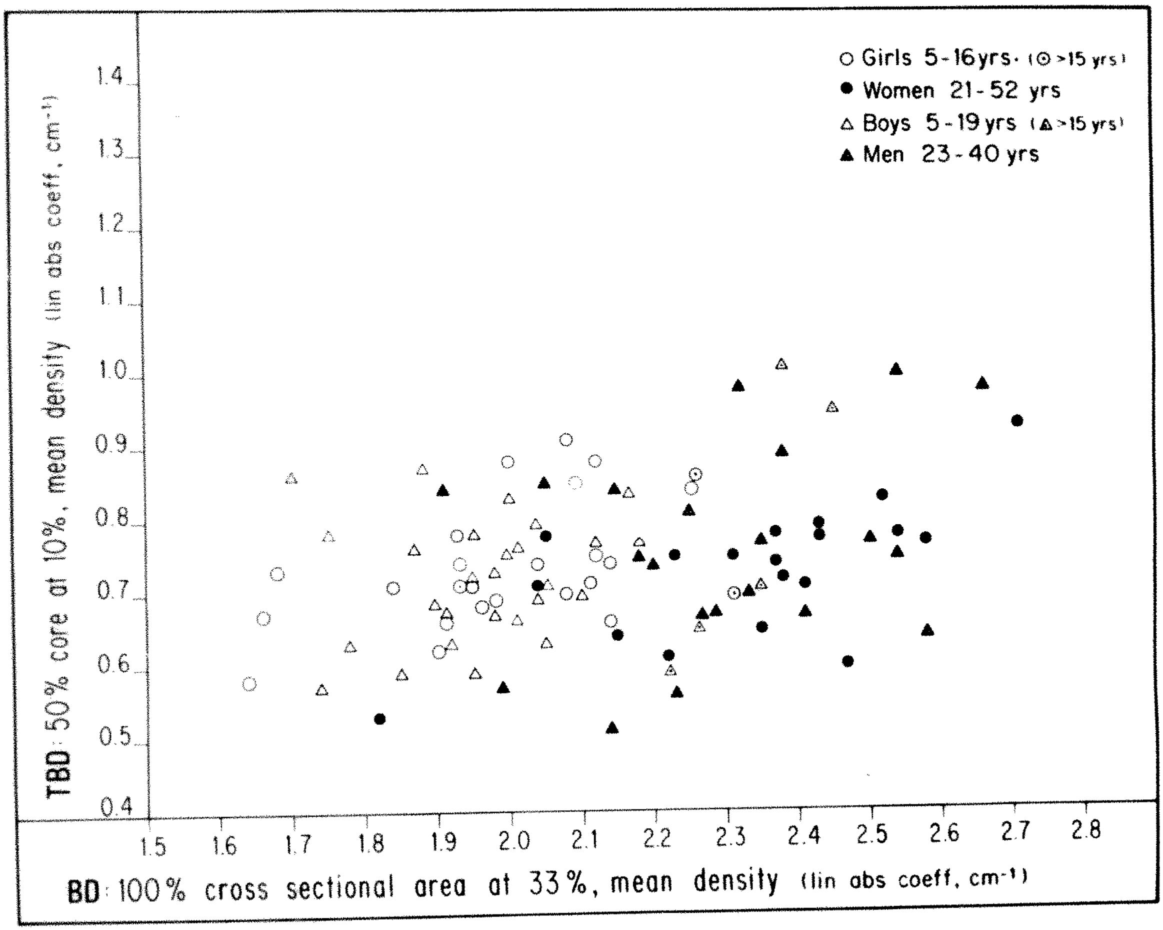

Fig. 3.

Correlation between TBD and BD in children and adults.

Subjects and measuring sites

All adults measured in this study were healthy volunteers. The children's measurement group consists of healthy volunteers and patients from the Kinderspital. Patients in this group were drawn from both in- and out-patient populations attending the Childrens' Hospital for minor surgical or medical problems which are not known to influence bone mineralization. Additionally, subjects undergoing drug therapy were excluded from the study group. Normative data for age, height, weight and body surface area for the study groups are given in Figs. 2, 4 and 5 and Table V. Body surface area was determined using the nomograms of Hannon and DuBois (cited in Crawford *et al.*, 1950).

Two γ-ray CT bone measurements are made for the radius; one at 10% and one at 33% of ulna length measured from the styloid process. Ulna length is measured using a special device and is defined as the largest distance between the olecranon and the palpable tip of the styloid process of the ulna when the arm is in extreme flexion (Fig. 1). To the present time only data for the radius have been analysed. In all cases γ-ray CT bone measurements were made for the dominant arm.

Statistical methods

The one- and two-tailed t-tests and Hottelling's t^2-test were applied to data to determine the significance of differences in mean values.

Definitions and abbreviations

The parameter obtained in these bone density measurements is the mean linear absorption coefficient with dimension cm^{-1}. No correction is made for the γ-ray absorption by soft tissue within the bone cross-section, and no attempt has been made to convert the measured bone density values to other

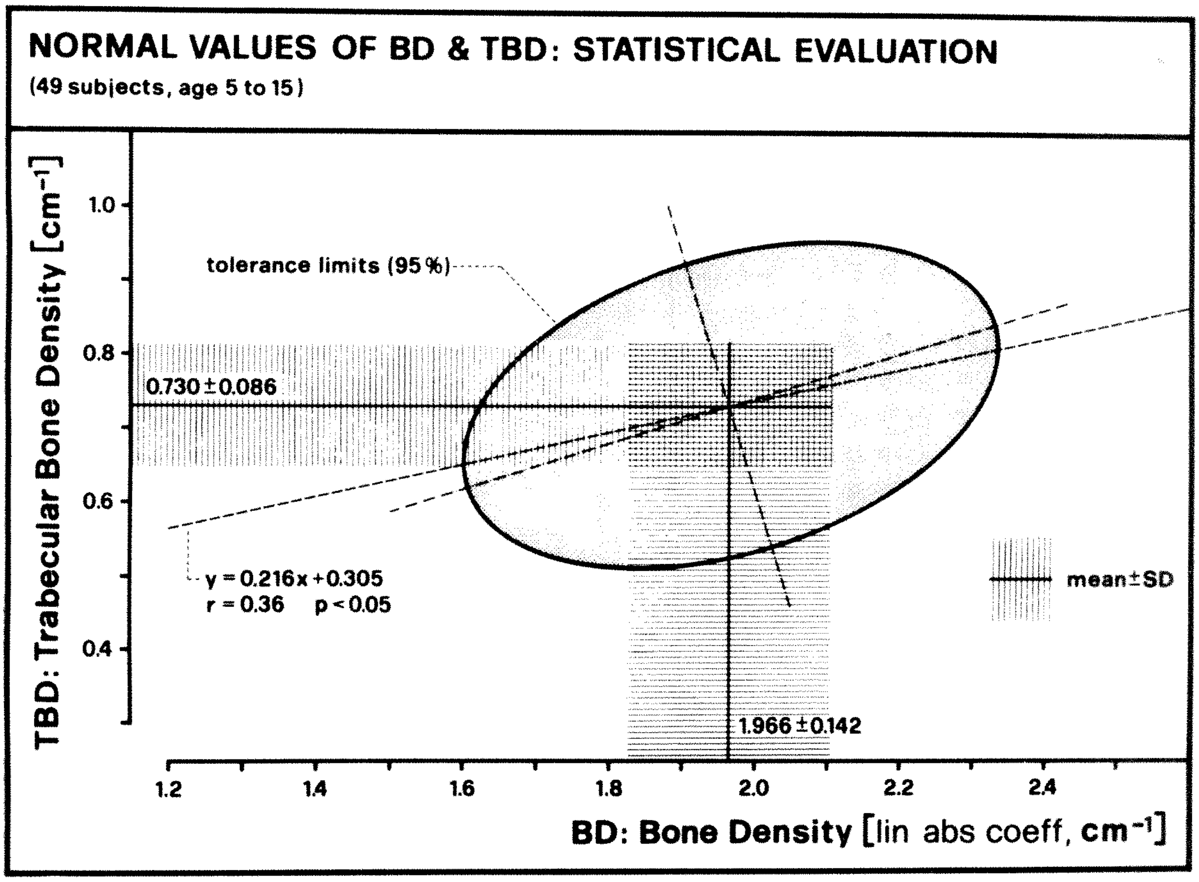

Fig. 4.

Graphical representation of the statistical evaluation of the normal values of TBD and BD in all children (girls and boys) aged 5 to 15 years. The ellipse gives the 95% tolerance limits; the regression function indicates the correlation between TBD and BD.

dimensions (*e.g.* mineral content per unit bone volume). The following nomenclature is used:

(1) Trabecular Bone Density (TBD) is the mean linear absorption coefficient for the 50% core of the radius at the 10% ulna length site.

(2) Bone Density (BD) is the mean linear absorption coefficient for the total cross-section of the radius at the 33% ulna length site. This parameter represents the relative amount of compact bone in the total cross-sectional area (=relative cortical area, Garn, 1970).

(3) Cross-Sectional Area (CA) is the total area of the radius at the 33% ulna length site, and has a dimension of cm^2.

(4) Total absorption (TA) is the sum of all measured linear absorption coefficients within the bone cross-section multiplied by the pixel size. It has the dimension (lin abs coeff., cm^{-1}), (cm^2)=cm. This parameter, which is calculated only for the radius at the 33% ulna length site, correlates most closely with the mineral content of the bone.

Results

In vivo reproducibility (inter-assay variability)

Full details of our extensive study of *in vivo* reproducibility, and of results we obtained in theoretical modelling and in measurements on bone phantoms have been reported (Elsasser, 1977).

To estimate the influence of motion artifacts during the five-minute scanning procedure, and the error associated with subject repositioning, serial measurements were made on a normal healthy man during a 50-day period. The results of this study are given in Table I. The smallest variation is in the measured TBD values (CV=±1.26%). The variation in parameters measured at the 33% site are slightly larger (CV=±1.62% for BD, ±2.16% for CA and ±1.84% for TA).

TABLE I

REPRODUCIBILITY IN VIVO (INTER-ASSAY VARIABILITY): VALUES OF TBD, CA, BD, AND TA IN TEN CONSECUTIVE MEASUREMENTS DURING A PERIOD OF 50 DAYS IN A NORMAL HEALTHY MAN, 32 YEARS OLD.

	TBD (cm^{-1})	CA (cm^2)	BD (cm^{-1})	TA (cm)
Mean ± SD	0.963 ± 0.012	1.665 ± 0.036	2.405 ± 0.039	4.010 ± 0.074
Coefficient of variation (%)	1.26	2.16	1.62	1.84
Range	0.95–0.98	1.60–1.71	2.33–2.47	3.87–4.10

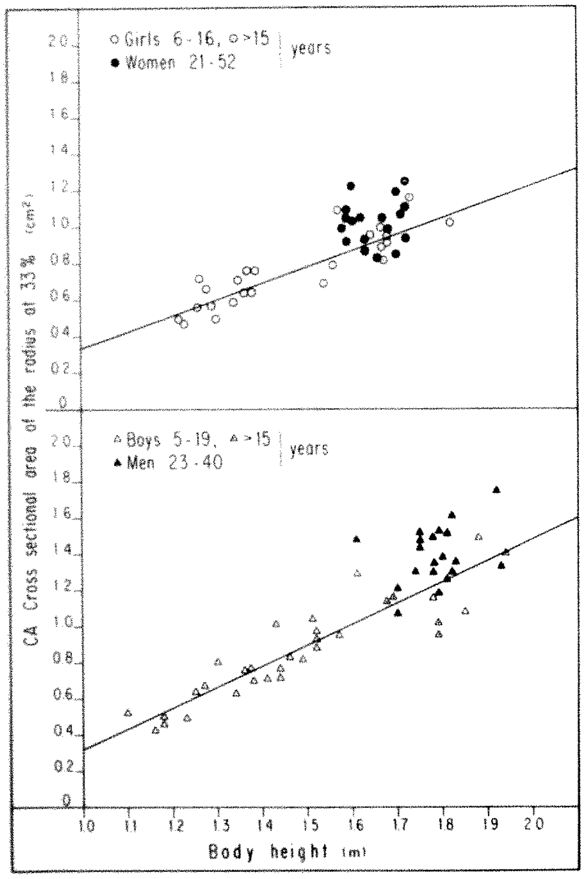

FIG. 5.

Correlation between CA and body height in male and female subjects. The lines are calculated regression functions for girls and boys below the age of 15 years, as given in Table III.

The explanation for the smaller error at the 10% site is that, at this site, TBD changes only a little with increasing distance from the styloid process and is rather homogenous throughout the cross-section (Elsasser, 1977). Thus, slight movements during the measurement, or a repositioning error, influences the result much less than is the case for the determination of BD, CA and TA at the 33% measurement site.

Differences between right and left arms

In our study, with only a small number of subjects, the left-right differences in TBD and BD generally do not reflect a dominant side (Table II). However, TA is significantly lower ($p < 0.05$) in the non-dominant arm (Table II), reflecting the smaller size of the non-dominant radius. The difference in CA between dominant and non-dominant arm is not statistically significant. However, there is a tendency for CA to be smaller in the non-dominant arm, and lack of statistical significance may be due to the greater inter-assay variability for this parameter.

Trabecular bone density (TBD)

The wide distribution of the TBD values as a function of age is shown in Fig. 2. There is no correlation between TBD and age in boys or girls below 15 years ($r = 0.076$, $r = 0.039$ respectively), or in adults. Using pooled data for the different age and sex groups no significant differences between any pair of mean values were found (Table IV).

Bone density (BD)

A considerable variability in BD is also seen in all age groups. It can be seen in Fig. 2 that BD is higher for adults than for children and higher for men than for women.

It appears that this increase in BD takes place at some time during or after puberty. Due to a lack of data on pubertal stage and bone age in our measurement group, children aged up to 15 years were considered together as one group and adults over 21 years as the other. Within each of these age groups there is no correlation of BD with age, regardless of sex; $r = 0.026$ for boys 5 to 15 years, and $r = 0.116$ for girls 6 to 15 years. If the pooled data of these groups (Table IV) are compared statistically, significant differences ($p < 0.001$) are found in BD between girls and women, girls and men, boys and women and boys and men. No differences exist between boys and girls or men and women.

Bone densitometry using computed tomography. Part I

TABLE II

DIFFERENCES BETWEEN TBD, CA, BD, AND TA OF LEFT AND RIGHT AND DOMINANT AND NON-DOMINANT RADIUS

Deviation of left from right		Deviation of non-dominant from dominant			
	TBD	TBD	CA	BD	TA
Number of subjects examined	19	14	10	10	10
Mean ± SD (%)*	+0.67 ± 3.81	+0.57 ± 4.08	−3.32 ± 8.31	+0.57 ± 6.69	−4.21 ± 4.66
Range (%)*	−5.77–+8.00	−8.00–+7.5	−18.80–+7.35	−9.09–+9.77	−13.75–+4.17
P†	NS	NS	NS	NS	< 0.05

*The values given are the %-deviations.
†P-values from the one-tailed t-test.

TABLE III

REGRESSION STATISTICS FOR THE CORRELATION BETWEEN CA ($=y$) AND BODY SIZE PARAMETERS ($=x$)

	Girls Aged 6 to 15 years 22 subjects	Boys Aged 5 to 15 years 27 subjects	Women Aged 21 to 53 years 18 subjects	Men Aged 23 to 39 years 16 subjects
Body weight (kg)	$y=0.015x+0.219$ $r=0.847$ $P<0.001$	$y=0.016x+0.227$ $r=0.940$ $P<0.001$	$y=0.012x+0.360$ $r=0.538$ $P<0.02$	$y=0.010x+0.680$ $r=0.488$ $P<0.05$
Height (m)	$y=0.892x-0.548$ $r=0.883$ $P<0.001$	$y=1.170x-0.855$ $r=0.911$ $P<0.001$	$y=0.260x+0.594$ $r=0.112$ NS	$y=0.760x+0.119$ $r=0.357$ NS
Body surface area (m^2)	$y=0.634x-0.014$ $r=0.879$ $P<0.001$	$y=0.787x-0.126$ $r=0.954$ $P<0.001$	$y=0.596x+0.063$ $r=0.455$ NS	$y=0.516x+0.424$ $r=0.425$ NS

$r=$correlation coefficient. In each group all calculations were made on the same subjects.

TABLE IV

NORMAL VALUES OF TBD, BD, AND TA WITHIN DIFFERENT AGE GROUPS

	Girls Aged 6 to 15 years	Boys Aged 5 to 15 years	Women Aged 21 to 53 years	Men Aged 23 to 49 years
TBD (cm^{-1})				
Number of subjects	22	27	19	35
Mean ± SD	0.738 ± 0.087	0.724 ± 0.086	0.724 ± 0.089	0.790 ± 0.144
Coefficient of variation	11.85%	11.84%	12.28%	18.25%
Range	0.58–0.91	0.59–0.87	0.53–0.93	0.57–1.04
BD (cm^{-1})				
Number of subjects	22	27	18	25
Mean ± SD	1.979 ± 0.163	1.955 ± 0.124	2.319 ± 0.215	2.284 ± 0.199
Coefficient of variation	8.26%	6.34%	9.25%	8.70%
Range	1.64–2.25	1.70–2.18	1.82–2.71	1.91–2.66
TA (cm)				
Number of subjects	22	27	18	24*
Mean ± SD	1.493 ± 0.388	1.581 ± 0.471	2.377 ± 0.170	3.260 ± 0.433
Coefficient of variation	25.98%	29.82%	7.17%	13.27%
Range	0.893–2.183	0.903–2.412	2.074–2.646	2.483–4.194

*Aged 23 to 39 years.

Correlation between trabecular bone density (TBD) and bone density (BD)

Because of the considerable variation in both TBD and BD in normal subjects, and the difficulty in establishing limits for parameter values in pathologic states, we have investigated possible correlations between TBD and BD. Figures 3 and 4 indicate that there are identifiable areas in the TBD/BD plane for normal children and adults. A linear correlation between TBD and BD ($r=0.36$, $p<0.05$) is found for children. The distributions of the values for the different age groups have been compared using Hottellings t^2-test. A highly significant difference between children and adults ($p<0.001$) was found, but no significant differences between girls and boys below the age of 15 years or between women and men.

Cross-sectional area (CA) of the radius at the 33% ulna length site

Figure 5 shows the correlation between CA and body height in children and adults. The regression lines for boys and girls are not significantly different from each other. Figure 6 shows CA in relation to body weight for children and for adults. The analytic expressions for the regression lines in Figs. 5 and 6 are given in Table III. There are no significant differences between boys and girls, but a highly significant difference between women and men ($p<0.001$). In relation to body height and weight CA is higher for men than for women. But since height and weight distributions are not the same for both sexes it cannot be determined whether this is due to the different statures or other sex-specific influences.

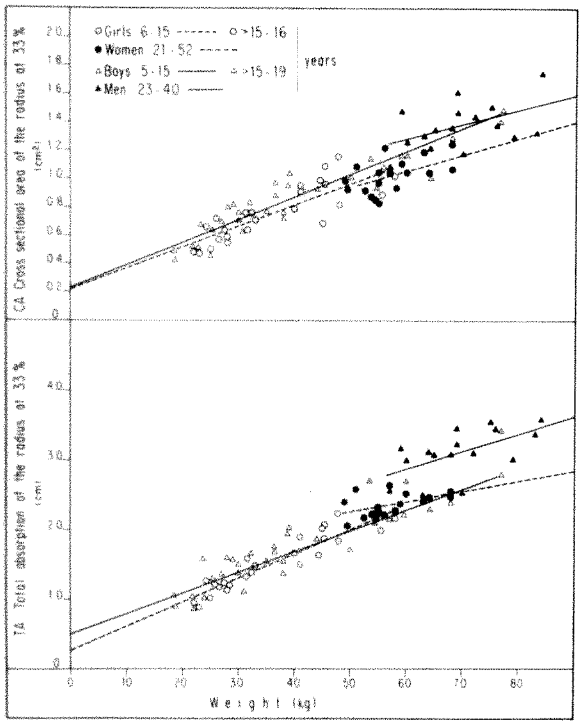

FIG. 6.

Correlation between TA and body weight, and between CA and body weight in children below the age of 15 years and adults, as given in Tables III and VI.

Total absorption (TA) of the radius at the 33% ulna length site

The distribution of TA values with age is shown in Fig. 7. Pooled data for the different age groups are summarized in Table IV. The variability in TA is particularly high for the children's groups due to the large differences in body size. The mean values of TA for men and for women are significantly different ($p<0.001$). Correlations between TA and anthropometric data have been made for each of the four subject groups. The regression functions and correlation coefficients for TA versus body height, body weight and body surface area are given in Table VI. The quotients of TA divided by each of these body size parameters have also been computed (Table V). In children there is a high correlation between TA and all body-size parameters, especially the body surface area (Table VI). In adults TA correlates best with body weight for both women and men, followed by body surface area. The correlation between TA and body height is low and not sex dependent. The distribution of TA versus body weight, and the corresponding regression lines for the different sex and age groups, are shown in Fig. 6.

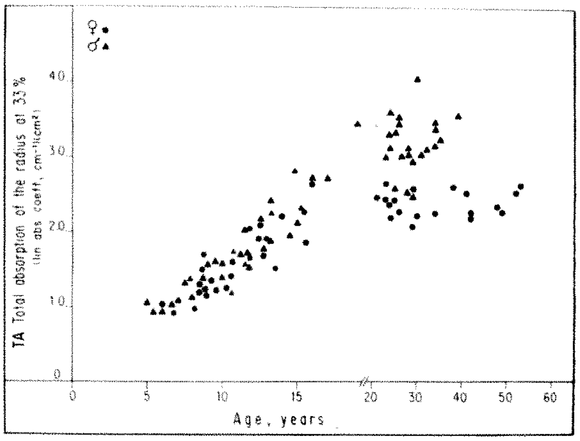

FIG. 7.

Distribution of TA according to age and sex.

TABLE V

DISTRIBUTION OF BODY SIZE PARAMETERS AND THEIR RELATIONS TO TA

	Girls Aged 6 to 15 years 22 subjects	Boys Aged 5 to 15 years 27 subjects	Women Aged 21 to 53 years 18 subjects	Men Aged 23 to 39 years 16 subjects
Body surface area (m^2) Mean ± SD Coefficient of variation Range	1.194 ± 0.256 21.45% 0.87–1.72	1.197 ± 0.310 25.90% 0.77–2.01	1.613 ± 0.093 5.80% 1.47–1.80	1.844 ± 0.139 7.51% 1.60–2.10
Body weight (kg) Mean ± SD Coefficient of variation Range	35.18 ± 10.50 29.85% 22.0–57.8	36.25 ± 14.79 40.79% 18.5–77.0	57.1 ± 5.7 9.90% 49–68	69.1 ± 8.2 11.28% 59–84
Body height (m) Mean ± SD Coefficient of variation Range	1.448 ± 0.183 12.64% 1.22–1.82	1.428 ± 0.199 13.94% 1.10–1.88	1.650 ± 0.053 3.20% 1.58–1.72	1.783 ± 0.079 4.43 1.61–1.93
TA: body surface area (cm)(m^{-2}) Mean ± SD Coefficient of variation Range	1.243 ± 0.132 10.62% 1.015–1.466	1.312 ± 0.141 10.75% 1.048–1.592	1.468 ± 0.105 7.19% 1.360–1.730	1.691 ± 0.169 10.02% 1.364–1.979
TA: body weight (cm) (kg^{-1})(10^{-3}) Mean ± SD Coefficient of variation Range	42.98 ± 4.30 10.00% 36.09–52.64	45.35 ± 6.93 15.28% 34.34–57.73	41.60 ± 3.72 8.94% 36.98–50.87	45.06 ± 4.70 10.43% 36.24–53.68
TA: body height (cm) (m^{-1}) Mean ± SD Coefficient of variation Range	1.018 ± 0.167 16.40% 0.726–1.326	1.087 ± 0.192 17.66% 0.778–1.498	1.433 ± 0.108 7.50% 1.272–1.592	1.741 ± 0.179 10.22% 1.417–2.259

In each group all calculations were made on the same subjects.

TABLE VI

REGRESSION STATISTICS FOR THE CORRELATION BETWEEN TA ($=y$) AND BODY SIZE PARAMETERS ($=x$)

	Girls Aged 6 to 15 years 22 subjects	Boys Aged 5 to 15 years 27 subjects	Women Aged 21 to 53 years 18 subjects	Men Aged 23 to 39 years 16 subjects
Body weight (kg)	$y=0.035x+0.280$ $r=0.933$ $P<0.001$	$y=0.030x+0.511$ $r=0.926$ $P<0.001$	$y=0.015x+1.512$ $r=0.505$ $P<0.03$	$y=0.025x+1.399$ $r=0.589$ $P<0.01$
Body height (m)	$y=1.845x-1.180$ $r=0.871$ $P<0.001$	$y=2.186x-1.540$ $r=0.923$ $P<0.001$	$y=0.242x+1.964$ $r=0.077$ NS	$y=1.744x+0.005$ $r=0.400$ NS
Body surface area (m^2)	$y=1.392x-0.170$ $r=0.919$ $P<0.001$	$y=1.436x-0.138$ $r=0.944$ $P<0.001$	$y=0.743x+1.165$ $r=0.421$ NS	$y=1.253x+0.803$ $r=0.504$ $P<0.05$

r = correlation coefficient. In each group all calculations were made on the same subjects.

For girls and boys ⩽ 15 years the regression lines for TA versus all body size parameters do not differ statistically. For adults the regression lines TA versus body weight are significantly different between women and men ($p<0.001$). Since BD, CA and TA are directly related the higher TA values in men cannot be attributed to sex specific influences alone.

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DISCUSSION

Non-invasive, selective *in vivo* measurements of trabecular bone density have only recently been developed (Ruegsegger *et al.*, 1976; Exner *et al.*, 1976; Elsasser and Exner, 1977). In contrast with all other reported measurements of bone density using the photon absorption technique the γ-ray CT-method provides precise measurements of TBD since the true cross-sectional area of the bone is obtained rather than a rough estimate as in other techniques (*e.g.* Mazzess and Cameron, 1972; Boerner *et al.*, 1972).

The absorption in bone of γ rays from a ^{125}I source reflects the mineral content of the bone (Boerner *et al.*, 1972; Cameron *et al.*, 1968), but it also depends on mineral composition (Rassow, 1974). We have, therefore, not converted the measured linear absorption coefficients into other units, such as amount of mineral per unit bone volume, since such conversions imply an identical composition of the bone mineral. In addition, determination of the absolute absorption coefficients of the non-mineralized components within the bone cross-section measured are required. Even though the variations in mineral composition, and in the non-mineralized components of the bone might be small in the normal this cannot be assumed to be true for pathological conditions.

In the present study no correction has been made for the absorption of γ rays by bone marrow (average linear abs coeff $\sim$0.35 cm^{-1}). Instead of determining the actual area of cortical bone and evaluating the true cortical bone density (which for methodological reasons cannot yet be done with sufficient accuracy in small bones), only the mean density of the total cross-section is determined. The mean density of the radius at the 33% ulna length site (BD) however, correlates directly with the relative amount of compact bone within the cross-section ("relative cortical area" (Garn, 1970)). From the data presented in this report it is seen that between the ages 5 and 15 years TBD, BD, and also the size of the radius in relation to body height and weight are independent of age. In this age group no sex differences exist for any of these parameters. When the size of the radius is considered in relation to body height and weight for the age groups—up to 15 years and above 21 years—a definite change is seen for men after puberty but not for women; men exhibit a much larger increase in CA than women. The ratios between CA and body height and weight are about the same for women as for girls (Figs. 5 and 6). In the present study it cannot be determined whether this relative increase of CA in the male takes place during final growth or after the longitudinal growth has ceased. The latter situation appears more likely judging by the results shown in Fig. 5. Bone density (BD) increases between puberty and adulthood. This can be due to an increased density of the cortical bone itself or to an increase in relative cortical area. We have assumed that it is due to increased cortical area, since it is known from many studies on metacarpals (*e.g.* Garn and Wagner, 1969), that the relative cortical area still increases when the sub-periosteal apposition has ceased and maximum cross-sectional area has been established. It should be noted that BD is the same for women and men.

The results shown in Figs. 3 and 4 suggest a proportionality of TBD and BD. For children this finding is supported by the regression statistics. In adults higher values of TBD tend likewise to be associated with higher values of BD. Hahn *et al.* (1974) obtained a similar relationship between "compact bone mineral content" and "trabecular bone mineral content" on the basis of photon absorption measurements of the diaphyseal and metaphyseal bone mass of the forearm. Boerner *et al.* (1972) studied the relationship between cortical thickness and estimated trabecular bone density of the metacarpal bones and reported similar results. However, neither of these two groups were actually measuring trabecular and compact bone mass or density separately.

Measurements of total absorption have been the basis of many investigations of bone mineral content (*e.g.* Mazzess and Cameron, 1971; 1972; Boerner *et al.*, 1972). The increase of bone mineral content with growth, and its large variability, make it more difficult to identify abnormal states of mineralization in children than in adults. To overcome this difficulty, Mazzess and Cameron (1971) correlated the bone mass with body size, but only with height and weight separately and only in children 6 to 14 years old. It is not surprising that both these parameters give a good correlation with bone mass since both are highly inter-related. Our regression statistics on TA, and its relation to height, body weight and body surface area, show high correlation coefficients for each of these parameters. It is uncertain whether weight or height plays the more important role with regard to TA and we therefore recommend the use of surface area as reference parameter in order to minimize false interpretation, especially in cases of abnormal body weight.

In adults, where CA and TA correlate best with body weight, no significant correlation with height is observed. Weight therefore seems to be the determining factor for the bone mass of the radius in adults. This result is somewhat surprising since physical activity would be expected to have a strong influence on bone mass, yet, in our subjects, higher weight was certainly not related to more physical activity. However, the differences between the dominant and non-dominant humerus in the study of Watson (1973), and in the radius in our series, suggest a positive influence of physical activity on bone size and mass.

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REFERENCES

BOERNER, W., GREHN, S., RAUH, E., and SEYBOLD, K., 1972. Altersphysiologische und pathologische Veränderungen der Dichte und Dicke des Fingerknochens. Radiologische Messungen mit einem ^{125}I-Profilscanner an 223 Frauen. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin, 116*, 552–558.

BURCKHARDT, L., 1954. Ueber Umbau und Strukturtypen der Wirbelkörperspongiosa als Ausdruck allgemeiner Gesetzmässigkeiten der Knochenmodellierung. *Verhandlungen der Deutschen Gesellschaft für Pathologie, 17*, 250–259.

CAMERON, J. R., and SORENSON, J. A., 1963. Measurement of bone mineral in vivo: an improved method. *Science, 142*, 230–232.

CAMERON, J. R., MAZZESS, R. B., and SORENSON, J. A., 1968. Precision and accuracy of bone mineral determination by direct photon absorptiometry. *Investigative Radiology, 3*, 141–150.

COHN, S. H., ELLIS, K. J., ZANZI, I., LETTERI, J. M., and ALOIS, J., 1973. Correlation of radial bone mineral content with total-body calcium in various metabolic disorders. In *Proceedings of the International Conference on Bone Mineral Measurement*, DHEW Publ., (NIH), 75-683, 39–50.

CRAWFORD, J. D., TERRY, M. E., and ROURKE, G. M., 1950. Simplification of drug dosage calculation by application of the surface principle. *Pediatrics, 5*, 783–790.

ELSASSER, U., 1977. Quantifizierung der Spongiosadichte an Röhrenknochen mittels Computertomographie. Doctoral Thesis, Federal Institute of Technology, Zurich (Dissertation ETH 5874).

ELSASSER, U., and EXNER, G. U., 1977. Application of computed tomography in bone mineral analysis (Abstract). *Federation Proceedings, 36*, 495.

EXNER, G. U., GNEHM, H. P., PRADER, A., ELSASSER, U., RUEGSEGGER, P., and ANLIKER, M., 1976. Bone densitometry with the aid of computer-assisted tomography (CAT). *Pediatric Research, 10*, 892.

GARN, S. M., and WAGNER, B., 1969. The adolescent growth of the skeletal mass and its implications of mineral requirement. In *Adolescent Nutrition and Growth*, ed. F. P. Heald, pp. 139–161 (Appleton-Century-Crofts, New York).

GARN, S. M., 1970. *The Earlier Gain and the Later Loss of Cortical Bone* (C. C. Thomas, Springfield).

HAHN, T. J., BOISSEAU, V. C., and AVIOLI, L. V., 1974. Effects of chronic corticosteroid administration on diaphyseal and metaphyseal bone mass. *Journal of Clinical Endocrinology and Metabolism, 39*, 274–282.

MAZZESS, R. B., and CAMERON, J. R., 1971. Skeletal growth in school children: maturation and bone mass. *American Journal of Physical Anthropology, 35*, 339–407.

1972. Growth of bone in school children: comparison of radiographic morphometry and photon absorptiometry. *Growth, 36*, 77–92.

MEEMA, H. E., 1973. Cortical bone atrophy and osteoporosis as a manifestation of aging. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 89*, 1287–1295.

RASSOW, J., 1974. Systematische Fehler bei der Mineralgehaltsbestimmung im Knochen. *Röntgenforschung, 121*, 77–86.

RUEGSEGGER, P., NIEDERER, P., and ANLIKER, M., 1974. An extension of classical bone mineral measurements. *Annals of Biomedical Engineering, 2*, 194–205.

RUEGSEGGER, P., ELSASSER, U., ANLIKER, M., GNEHM, H. P., KIND, H. P., and PRADER, A., 1976. Quantification of bone mineralization with the aid of computerized tomography. *Radiology, 121*, 93–98.

WATSON, R. C., 1973. Bone growth and physical activity in young males. In *Proceedings of the International Conference on Bone Mineral Measurement*, DHEW Publ. (NIH), 75-683, 380–386.

1979, *British Journal of Radiology*, *52*, 24–28

Bone densitometry using computed tomography

Part II: increased trabecular bone density in children with chronic renal failure*

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ABSTRACT

The method of gamma-ray computed tomography (γ-ray CT) bone densitometry described in the preceding article provides selective determination of trabecular bone density (TBD), the relative amount of compact bone (bone density, BD), and the total absorption (TA) within a bone cross section. Seven of nine children with chronic renal failure (CRF), and selected only on the basis of their serum creatinine value (> 5 mg/100 ml), had increased TBD values above the normal range, whereas the other bone mineral parameters were normal. Radiographic signs of secondary hyperparathyroidism (subperiosteal erosions, cysts) were reported in the five patients with the highest TBD values, whereas the subjective diagnosis of osteosclerosis reported in three of these five and in one other patient correlated less well with the TBD increases. However, this is the first report of an objective, non-invasive documentation of the radiological finding of osteosclerosis in CRF. It also explains why methods for bone mineral measurements used previously, such as a photon absorptiometry which provides only a parameter equivalent to TA, failed to reveal increases in bone mineral content in renal osteodystrophy even when signs of osteosclerosis were present. Thus, γ-ray CT helps to document objectively the degree of osteosclerosis and its location.

Renal osteodystrophy is a term used to describe skeletal abnormalities associated with chronic renal insufficiency. These abnormalities include rickets, osteomalacia, osteosclerosis, metastatic calcifications and osteitis fibrosa cystica all of which involve impaired bone metabolism and disturbed mineralization (*e.g.* Kleeman *et al.*, 1970; Resnick and Niwayama, 1976). Several non-invasive methods of bone mineral analysis are available (*e.g.* radiological surveys, photon absorptiometry, *in vivo* neutron activation analysis), and these have been widely used for the study of renal osteodystrophy (Resnick and Niwayama, 1976; Crawford *et al.*, 1954; Zimmerman, 1962: Haust *et al.*, 1964; Johnson *et al.*, 1967; Cohen *et al.*, 1970; Meema *et al.*, 1972; Cohn *et al.*, 1973; Dalen and Alvestrand, 1973; Griffiths and Zimmerman, 1973; Genant *et al.*, 1975; Campos *et al.*, 1976; Overton *et al.*, 1976; Harrison *et al.*, 1977; Ferran *et al.*, 1977). However, none of these methods give information concerning the mineral distribution within the bone nor do they permit a differentiation between compact and trabecular bone.

PATIENTS AND METHODS

Patients

All patients with chronic renal failure and a serum creatinine above 5.0 mg/100 ml and not on dialysis, who attended the Kinderspital, Zurich during the period from December 1975 to January 1977, were informed about the study and were asked to participate. Nine patients satisfying the selection criteria were subsequently measured using the γ-ray CT-technique. Serum analyses and X rays were made independently from this study.

Data on these patients, including diagnosis, progression of renal failure, treatment, and serum analyses at the time of the measurements, are given in Table I. Data on height and weight are included in Table II.

Bone densitometry

Determinations of bone density (BD), cross-sectional area (CA) and total absorption (TA) of the radius of the dominant arm were made as described in Part I. The quantification of trabecular bone density (TBD) of the radius at 10% ulna length in three patients (Nos. 1, 5, 8) had to be based on a core smaller than the usual 50% of the cross-sectional area of the radius since their cortical bone area exceeded 50%. This situation has not been encountered so far in the normal child or adult.

Evaluation of X rays

Bone age was determined according to Greulich and Pyle (1950). Subperiosteal diameter (T) and cortical width (C) of the second metacarpal were measured according to Garn (1970). For the diagnosis of signs of osteitis fibrosa cystica, of rickets and

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TABLE I

Patients, renal disease, vitamin D_3–treatment, progression of renal failure, and serum values

Pt*	Sex	Age	BA	Dx	Vit D_3–treatment		Documented period of creat increase before CT (y:m)		Serum values at time of CT mg/100 ml			Prot g/100 ml	alk P-ase IU
		y:m	y:m		Dose units/day	Duration y:m	> 2 mg/100 ml	> 5 mg/100 ml	Creat	Ca	P		
1	M	5: 9	4	H	none		-	-	5.6	8.6	4.3	6.4	201
2	F	11: 8	8:10	H,A,Hn	4000	: 9	2	1	7.4	8.6	4.3	6.6	125
3	M	13: 8	11: 6	D	5000	: 6	4	: 6	11.6	8.8	6.1	6.3	162
4	F	14:10	13: 6	H	none		12	2	7.8	9.2	5.5	7.0	200
5	M	13: 3	9	A,Hn	3000	3	7	1	8.5	9.7	6.2	6.5	140
6	M	14:10	11: 6	Hn	4000	1: 3	4	: 2	5.7	8.7	4.9	6.5	100
7	F	14: 5	13: 6	H	10000	: 9	–	1	5.5	9.7	3.8	7.5	152
8	M	10: 5	11: 6	G	4000	: 3	: 9	: 2	7.9	9.0	5.2	6.2	93
9	F	9:11	11	G	none		:11	: 6	10.3	7.9	7.8	6.5	230

*Pt–patient; CT–computed tomography; Age–chronological age; BA–bone age; Dx–diagnosis; Creat–creatinine; Ca–calcium; P–phosphorous; Prot–protein; alk P-ase–alkaline phosphatase; y–years; m–months; H–renal hypoplasia; A–renal aplasia; D–renal dysplasia; Hn–hydronephrosis; G–glomerulonephritis.

TABLE II

Body size and bone mineral parameters of the patients presented in Table I

Pt*	Ht cm	Wt kg	SA m^2	TBD cm^{-1}	CA cm^2	BD cm^{-1}	TA:SA $cm:m^2$
1	108	15	0.67	1.28	0.44	1.67	1.097
2	133	27	1.01	1.18	0.58	1.86	1.068
3	143	34	1.16	1.08	0.65	1.95	1.093
4	132	33	1.08	1.04	0.67	2.29	1.421
5	126	25	0.93	1.02	0.64	1.89	1.301
6	144	49	1.37	0.99	0.87	2.10	1.334
7	141	35	1.18	0.92	0.67	1.91	1.084
8	144	31	1.13	0.90	0.75	1.97	1.303
9	141	33	1.14	0.82	0.75	1.90	1.250
Mean ±SD				1.03 ±0.14		1.95 ±0.17	1.217 ±0.133
Normal values of boys and girls 5 to 15 years, n=49							
Mean ±SD				0.73 ±0.09		1.97 ±0.14	1.281 ±0.140
P				<0.001		NS	NS

*Pt–patient; Ht–body height; Wt–body weight; SA–body surface area. P-values from the two-tailed t-test indicate that TBD is significantly increased in children with chronic renal failure, whereas the other bone mineral parameters are normal.

the presence of osteosclerosis the X rays of the hand and wrist were examined by a paediatric radiologist who had no knowledge of the results of the bone densitometry.

Serum analyses

Calcium was determined by atomic absorption (9.0 to 11.0 mg/100 ml), phosphorous according to Itaya and Ui (1966) (4.0 to 6.0 mg/100 ml), creatinine according to Devries and van Daetselaar (1955) (0.2 to 1.0 mg/100 ml), and alkaline phosphatase activity using the kit Art. 1020 of the F. Hoffmann-La Roche & Co. AG Diagnostics, Basel, Switzerland (30 to 140 IU). Protein was measured by the biuret method (6.0 to 7.5 mg/100 ml). The values in parentheses are considered normal for the age group of our patients.

Statistical analyses

Since most patients had small stature, metacarpal bone measurements were evaluated in relation to body height in terms of the standard deviation score (SDS). The SDS of T and C for chronological age were determined using the normal values given by Garn (1970) while the SDS of height for chronological age were determined on the basis of values from a longitudinal growth study in Zurich.* We are aware of the problems inherent in comparisons of data obtained from different populations, but we nevertheless wish to provide information which permits a preliminary comparison between the conventional methods of the analysis of the hand and wrist X rays and those of bone densitometry of the radius.

TABLE III

Evaluation of the x rays of the hand and wrist of the patients presented in Table I

Pt*	Bone cysts and/or subperiosteal erosions	Osteosclerosis	Rickets
1	+	+	+
2	+	+	+
3	+	—	—
4	+	+	—
5	+	—	+
6	—	+	—
7	—	—	—
8	—	—	—
9	—	—	—

*Pt = patient; + = present; — = absent.

For statistical analysis of differences observed the one-tailed and two-tailed t-test and Hotteling's t^2-test have been used.

Results

Bone densitometry

The results of the bone densitometry are presented in Table II and Fig. 1. When the TBD values of patients with chronic renal failure are compared with those of normal children (see Part I) the difference is highly significant ($p < 0.001$). If TBD is considered in relation to BD, all but two (Nos. 8 and 9) of the patients are clearly above the normal range (Fig. 1). This observation is corroberated by the t^2-test when TBD and BD distributions are compared between patients and normal children ($p < 0.001$). With regard to BD, CA in relation to body height

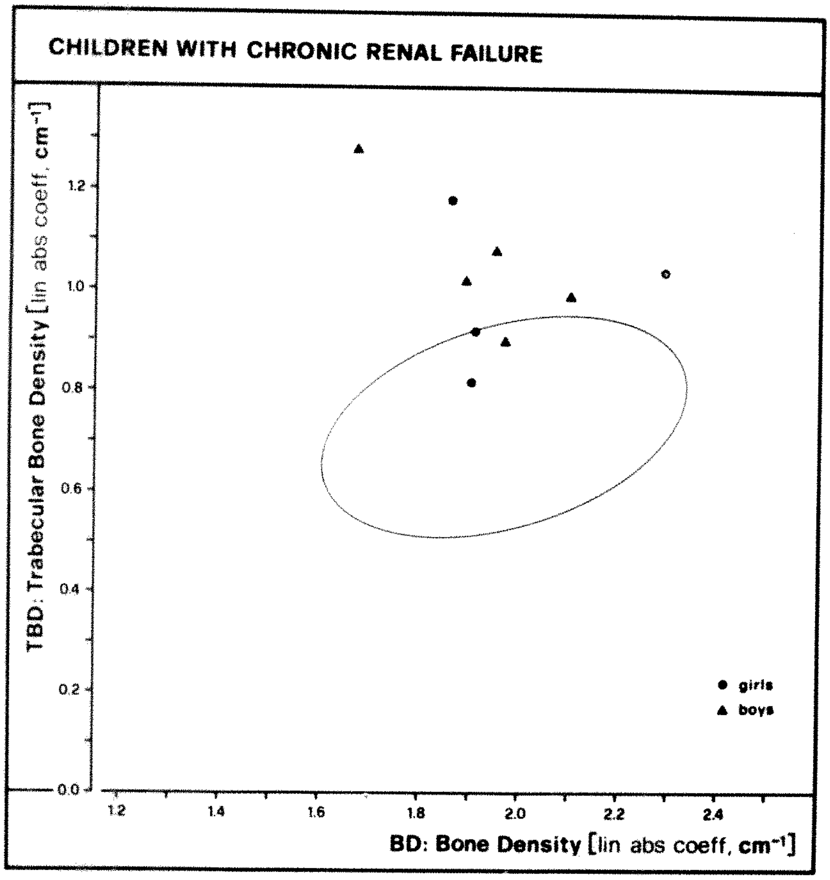

Fig. 1.

Values of TBD and BD of children with chronic renal failure. The ellipse gives the 95% tolerance limits for normal children aged five to 15 years.

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*In preparation.

TABLE IV

EVALUATION OF THE SUBPERIOSTEAL DIAMETER (T) AND OF THE CORTICAL WIDTH (C) OF THE SECOND METACARPAL BONE

Pt*	SDS Ht	T mm	SDS T	SDS T –SDS Ht	C mm	SDS C	SDS C–SDS Ht	SDS C–SDS T
1	−1.8	5.1	−1.7	+0.1	2.1	−1.9	−0.1	−0.2
2	−2.3	6.9	−0.6	+1.7	3.4	−1.2	+1.1	−0.6
3	−2.0	6.6	−2.4	−0.4	3.4	−2.4	−0.4	±0.0
4	−5.3	6.1	−2.7	+2.5	3.7	−2.1	+3.1	+0.6
5	−3.9	6.3	−2.7	+1.2	3.5	−2.0	+1.9	+0.7
6	−3.1	6.5	−3.0	±0.0	3.2	−3.0	+0.1	+0.1
7	−3.5	6.9	−1.4	+2.0	3.5	−2.5	+1.0	−1.0
8	+0.3	6.9	−0.8	−1.1	3.5	−1.0	−1.3	−0.2
9	+1.0	6.5	−0.5	−1.5	3.3	−0.5	−1.5	±0.0
Mean ±SD	−2.28 ±1.98		−1.77 ±0.99	+0.50 ±1.41		−1.84 ±0.79	+0.44 ±1.50	−0.01 ±0.50
P‡	<0.005		<0.001	NS		<0.001	NS	NS

*Pt–patient, SDS–standard deviation score, Ht–body height, T–subperiosteal diameter, C–cortical width.
‡P–value from the single tailed t test.
SDS–calculations indicate a normal size of the second metacarpal bone in relation to body height and a normal correlation between T and C.

and TA in relation to body surface area, no differences are found between patients and normal children.

X-ray analyses

The X-ray findings are summarized in Table III. Subperiosteal erosions and/or bone cysts were present in five patients, signs of rickets in three and signs of osteosclerosis in four. Values of T and C are shown in Table IV. All values are below normal relative to chronological age, but from comparison of the SDSs it is evident that, on average, all patients have normal correlations between T, C and body height. The normal correlation between C and T, with SDS-differences never exceeding −1.0 and +0.7, should be noted especially.

Serum analyses

The results of the serum analyses are summarized in Table I. Creatinine was above 5.0 mg/100 ml in all patients. Serum phosphorous tends to be higher and calcium lower than normal. With the exception of patient No. 2 alkaline phosphatase activity was high in all patients with signs of osteitis fibrosa cystica (subperiosteal erosions and/or bone cysts). In patient No. 7 alkaline phosphatase activity was increased without signs of osteitis fibrosa cystica. Protein was in the normal range in all patients.

DISCUSSION

The γ-ray CT measurements clearly show an increased density of the trabecular bone of the radius in seven of nine children with chronic renal failure. These trabecular bone density measurements are, to our knowledge, the first *in vivo* verification of radiographic findings of osteosclerosis as increases in trabecular bone density. The possible occurrence of osteosclerosis in uraemia is well accepted, but its reported incidence varies from zero (Johnson *et al.*, 1967) to 41% (Harrison *et al.*, 1977). Non-invasive methods for bone mineral determination used previously (photon absorptiometry) are not sufficiently sensitive to detect TA changes in bone mineral due to increases in TBD since they yield only parameters equivalent to TA. This may explain why such techniques failed to reveal increases in bone mineral content (*e.g.* Griffiths and Zimmerman, 1973; Overton *et al.*, 1976) even when radiographic signs of osteosclerosis were present (Genant *et al.*, 1975). Radiographic measurements of cortical thickness or cortical area in the metacarpals of patients with uremic osteosclerosis showed either normal (Meema *et al.*, 1972) or reduced values (Cohen *et al.*, 1970). The lack of precision in the radiographic identification criteria for osteosclerosis and osteoporosis may explain the discrepancy between the conventional X-ray diagnosis and the results of γ-ray CT in our patients. An experienced radiologist diagnosed osteosclerosis in four cases, while the other five he considered as normally mineralized or as being on the high normal side. In addition, radiographic evaluations of the second metacarpal of our patients never showed very high or low C in comparison with T. All parameters except TBD measured by γ-ray CT on the radius were normal. Admittedly no proof is given that long bones of the hand behave similarly to the radius with respect to mineralization, but it can be assumed from the similarities in anatomy and from the measurements of Boerner *et al.*, (1972) that they do.

An explanation for the TBD increase cannot as yet be given. We do not have enough information on whether TBD increases generally with protracted renal failure in children, or whether it depends on the disease causing uraemia (only two of the patients did not suffer from congenital renal malformations). Secondary hyperparathyroidism might play an important role, though not all patients had symptoms commonly attributed to this condition, such as elevated alkaline phosphatase activity and osteitis fibrosa cystica. Although we do not care to add to the theories regarding the relationship between uraemic osteodystrophy, parathyroid hormone activity and vitamin D metabolism (Cohen *et al.*, 1970; Genant *et al.*, 1975; Overton *et al.*, 1976; Reeve *et al.*, 1976; Labarrere and Mautalen, 1976), it is interesting to note that in two of our patients (Nos. 2 and 4) treatment with 1.25 $(OH)_2$ cholecalciferol (1 μg daily during five months) resulted in a normalization of the serum alkaline phosphatase activity and a complete remission of the radiological signs of osteitis fibrosa cystica. However, no significant changes of TBD, BD or TA were seen. Also, chronic haemodialysis did not result in significant changes after five and seven months in patients Nos. 3 and 8 respectively. This suggests that the different skeletal abnormalities occurring with chronic renal insufficiency may be caused by different events and may exist independently from each other. This also shows that it is necessary to study each parameter separately with the appropriate method for the question considered.

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REFERENCES

BOERNER, W., GREHN, S., RAUH, E., and SEYBOLD, D., 1972. Altersphysiologische und pathologische Veränderungen der Dichte und Dicke des Fingerknochens. Radiologische Messungen mit einem ^{125}I-Profilscanner an 223 Frauen. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin, 116*, 552–558.

CAMPOS, C., ARATA, R. O., and MAUTALEN, C. A., 1976. Parathyroid hormone and vertebral osteosclerosis in uremic patients. *Metabolism, 25*, 495–501.

COHEN, M. E. L., COHEN, G. F., AHAD, V., and KAYE, M., 1970. Renal osteodystrophy in patients on chronic hemodialysis. A radiological study. *Clinical Radiology, 21*, 124–134.

COHN, S. H., ELLIS, K. J., ZANZI, I., LETTERI, J. M., and ALOIA, L., 1973. Correlation of radial bone mineral content with total body calcium in various metabolic disorders. In *Proceedings of the International Conference on Bone Mineral Measurements*, DHEW Publ. (NIH), 75–683, 39–50.

CRAWFORD, T., DENT, C. E., LUCAS, P., MARTIN, N. H., and MASSIM, J. R., 1954. Osteosclerosis associated with chronic renal failure. *Lancet, 2*, 981–988.

DALEN, N., and ALVESTRAND, A., 1973. Bone mineral content in chronic renal failure and after renal transplantation *Clinical Nephrology, 1*, 338–346.

DEVRIES, L. A., VANDAETSELAAR, J. J., 1955. Bepaling van creatinine in serum volgens Volin. In *Klinische Diagnostik*, editors E. Gator and W. C. Graaf, 7th edn, pp.278 (H.E. Stenfert and N. V. Krose, Leiden).

FERRAN, J. L., LUCIANI, J. C., MEUNIER, P., and DUMAS, R., 1977. Ostéodystropie rénale de l'enfant. *Journal de Radiologie, d'Electrologie et de Médecine Nucléaire, 58*, 173–181.

GARN, S. M., 1970. *The earlier Gain and the Later Loss of Cortical Bone*, 15 and 45. (S. C. Thomas, Springfield).

GENANT, H. K., BARON, J. M., PALOYAN, E., and JOWSEY, J., 1975. Osteosclerosis in primary hyperparathyroidism. *American Journal of Medicine, 59*, 104–113.

GREULICH, W. W., and PYLE, S. I., 1950. *Radiographic atlas of skeletal development of the hand and wrists.* (Stanford University Press, Stanford, USA).

GRIFFITHS, H. J., and ZIMMERMAN, R. E., 1973. The role of photon absorptiometry in the diagnosis and follow-up of patients with renal failure. In *Proceedings of the International Conference on Bone Mineral Measurements*, DHEW Publ. (NHI) 75–683, 337–345.

HARRISON, J. E., MCNEILL, K. G., MEEMA, H. E., OREOPOULOS. D., RABINOVITCH, S., FENTON, S., and WILSON, D. R., 1977. Partial body calcium measurements on patients with chronic renal failure. *Metabolism, 26*, 255–265.

HAUST, M. D., LANDING, B. H., HOMSTRAND, K., CORRARINO, G., and SMITH, B. S., 1964. Osteosclerosis of renal disease in children. *American Journal of Pathology, 44*, 141–151.

ITAYA, K., and UI, M., 1966. A new micromethod for the colorimetric determination of inorganic phosphate. *Clinica Chimica Acta, 14*, 361–363.

JOHNSON, C., GRAHAM, C. B., and CURTIS, F. K., 1967. Roentgenographic manifestation of chronic renal disease treated by periodic hemodialysis. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 101*, 915–926.

KLEEMAN, C. R., MASSRY, S. G., COBURN, J. W., and POPOVITZER, M. M., 1970. Calcium and phosphorous metabolism and bone disease in uremia. *Clinical Orthopaedics and Related Research, 68*, 210–237.

LABARRERE, C. A., and MAUTALEN, C. A., 1976. Parathyroid activity and bone formation. *Metabolism, 25*, 135–138.

MEEMA, H. E., RABINOVICH, S., MEEMA, S., LLOYD, G. J., and OREOPOULOS, D. G., 1972 Improved diagnosis of acotemic osteodystrophy. *Radiology, 102*, 1–10.

OVERTON, T. R., SILVERBERG, D. S., GRACE, M., RIGAL, W. M., HIGGINS, M., BETTCHER, K. B., DOSSETOR, J. B., HARLEY, F., and DELUCA, H. F., 1976. Bone demineralization in renal failure: a longitudinal study of the distal femur using photon absorptiometry. *The British Journal of Radiology, 49*, 921–925.

REEVE, J., WILLIAMS, D., HESP, R., HULME, P., KLENERMAN, L., ZANELLI, J. M., DERBY, A. J., TREGEAR, G. W., PARSONS, J. A., 1976. Anabolic effect of low doses of a fragment of human parathyroid hormone on the skeleton in postmenopausal osteoporosis. *Lancet, 1*, 1035–1045.

RESNICK, D., and NIWAYAMA, G., 1976. Subchondral resorption of bone in renal osteodystrophy. *Radiology, 118*, 315–321.

ZIMMERMAN, H. B., 1962. Osteosclerosis in chronic renal disease. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 88*, 1152–1169.

1979, *British Journal of Radiology*, *52*, 29–33

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A rotating transducer real-time scanner for ultrasonic examination of the heart and abdomen

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ABSTRACT

A mechanical real-time ultrasonic scanner utilizing a rotating transducer head has been successfully applied clinically to visualize the heart and abdomen. The design features of this scanner are discussed. The small dimensions and the 90° field of view of the sealed oil-filled transducer head optimize visualization of the heart avoiding bone and lung. The single point of entry aspect of this scanner results in a good field of view from any point on the abdominal surface. For example, in upper abdominal studies the liver and kidney can be readily viewed. Rapid and thorough searching of the abdomen is easily carried out and good quality selected sections can be captured by optimizing frame rate and angle of view. In obstetrical applications the complete mature fetus can be visualized using the alternative large 180° field of view.

Real-time ultrasonic imaging allows visualization of dynamic structures and removes patient movement artifacts while scanning through static structures. The ultrasonic beam is rapidly moved by mechanical or electronic means to form the real-time images. This paper describes a mechanical real-time scanner which has been designed to overcome the anatomical problems encountered in clinical applications. By rotating standard transducers through a chosen sector, images are formed using a constant well defined beam shape at all angles in that sector.

Oscillating mechanical scanners have been developed for real-time echocardiography (Griffith and Henry, 1974; Flaherty *et al.*, 1967; McDicken *et al.*, 1974). A rotating transducer scanner in which the transducers are swept across the skin surface has been developed primarily for scanning the abdomen (Holm *et al.*, 1975). A rotating transducer scanner has also found application in visualizing superficial blood vessels. In this assembly the transducers are coupled to the patient's skin via a water bath (Barber *et al.*, 1974). Electronic real-time scanners take the form of linear arrays or phased arrays (Bom *et al.*, 1971; Kisslo *et al.*, 1976; Somer, 1968; Von Ramm and Thurstone, 1976). Electronic scanners have the advantage of having no moving parts. Ultrasonic access to the patient is often limited when linear arrays are employed due to gas, bone and difficulty in coupling to curved body surfaces. At present phased arrays are expensive and have a limited field of view.

Although the scanner described here is well suited to visualization of the abdomen it was initially designed for cardiac studies. A small point of entry device was desirable to avoid ribs, sternum and lung interfering with the ultrasonic beam while giving the freedom to visualize more than one plane of view simultaneously using multiple scanners. The restricted dimensions also allow two or more scanners to be used at adjacent intercostal spaces. It also retains the flexibility of scanning of a single transducer which has been used successfully in cardiac T-M mode scanning. The rotating transducer has been used successfully in cardiology, obstetrics and general abdominal scanning.

DESCRIPTION

A mechanical real-time rotating scanner was developed after investigating the feasibility of heart visualization using oscillating and rotating transducer techniques. The rotating head consists of four 1.5 cm diameter, 2.5 MHz transducers inserted into a 3 cm diameter wheel. Similar transducers are used in static B-scanning applications and are known to produce high quality images. The crystal faces are evenly spaced round the periphery of the wheel with an angular separation of 90°. The wheel rotates within an oil filled cylindrical cavity and electrical coupling to the transducers is via gold slip rings and brushes. Acoustic coupling to the patient is maintained by gel between the thin Perspex (Plexiglass) outer wall of the cavity and the skin. This avoids any moving parts coming into direct contact with the patient. Figure 1 shows the transducer head which is driven by a d.c. motor via a gearbox and belt-drive. The scanner is presented hand-held in Fig. 2.

The transducers are pulsed while they pass through the 90° sector of the head which is in contact with the patient. A 90° sector image is produced each time a transducer sweeps through this sector and therefore the frame rate is four times the angular velocity of the transducer head. This is varied by controlling the d.c. motor speed, and frame rates up to approximately 40 frames per second are possible. The pulse repetition frequency (PRF) of the A-scan

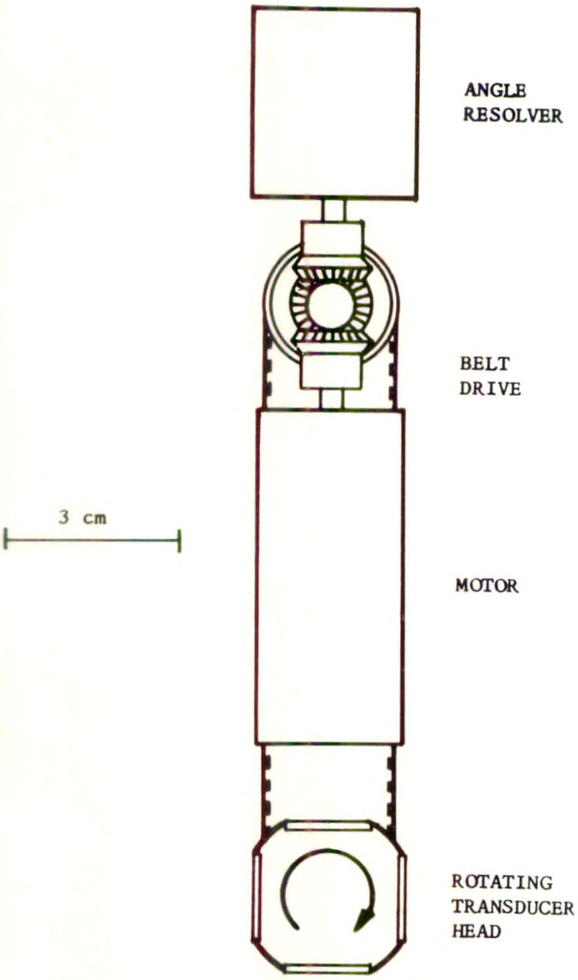

Fig. 1.
Schematic diagram of scanner components.

transmitter is 3000 Hz and therefore at 20 frames per second a 90° sector image contains 150 evenly spaced lines.

The angular position of the ultrasound beam is measured by a resolver which is driven in phase with the transducer head. This angular information is used to locate the individual lines of the image. Synchronization pulses are obtained from an opto-electronic timing device. The individual lines are written at the pulse repetition frequency on a gray scale display to generate a single sector image. These sectors are then refreshed at the frame rate and yield real-time gray scale images.

Discussion

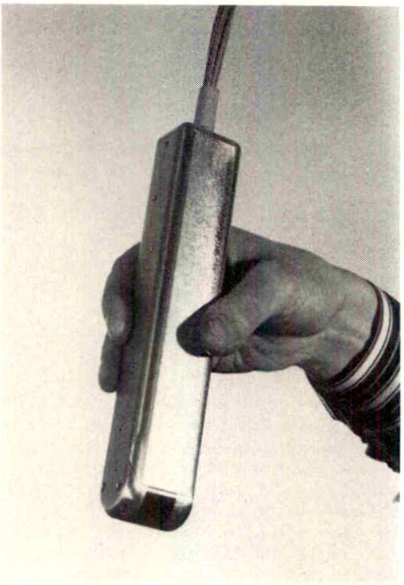

Fig. 2.
Scanner hand held.

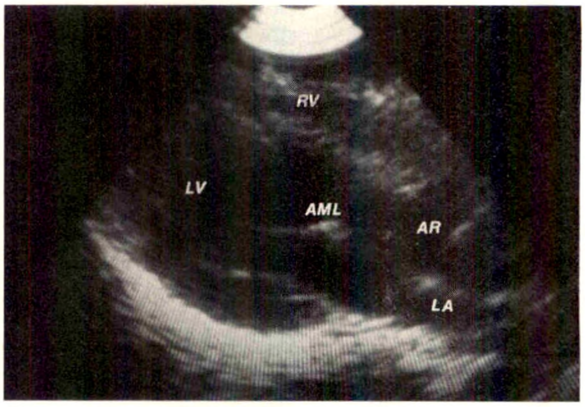

Fig. 3.
Longitudinal section of the heart corresponding to frame eight of Fig. 4 showing left ventricle (LV), right ventricle (RV), left atrium (LA), aortic root (AR), anterior mitral leaflet (AML), aortic valve, septum and endocardium in the left ventricle.

A 3 cm diameter wheel allows two scanners to operate at adjacent intercostal spaces. Preliminary tests simulating a 1.5 cm diameter transducer rotating within these dimensions showed that 50° to 80° sector images of the heart were feasible without rib interference. However, although sector angle is limited in heart visualization it need not be in other areas of application. If two opposing transducers are excited instead of four then a 180° sector is possible, the actual angle of view being determined by the acoustic contact made with the patient. Because of

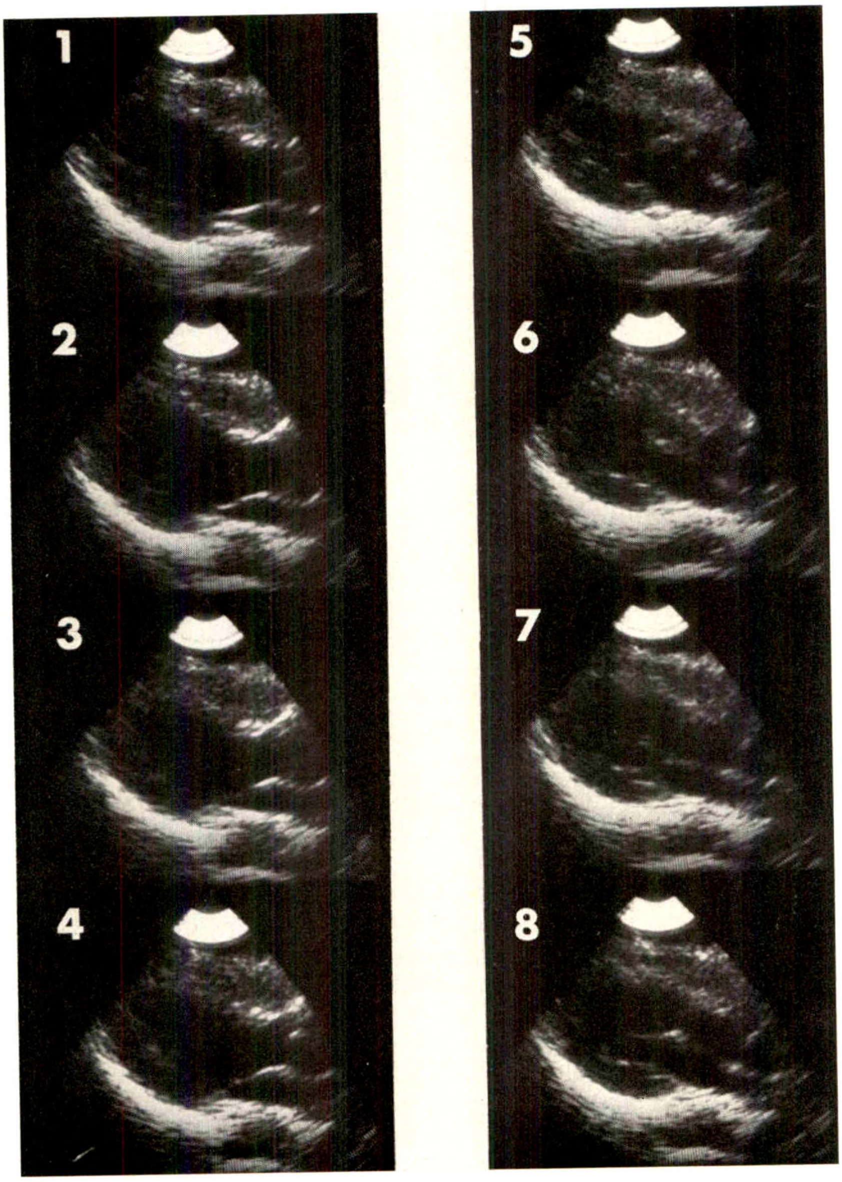

FIG. 4.

Series of eight successive cine frames at 1/10th second intervals showing the action of the longitudinal section of the heart.

the small diameter of the sealed head this can be in the range 120° to 150° for abdominal scans. Depression into the abdomen to increase contact angle does not mechanically load the rotating head and gel is not removed by any moving parts.

Used in this mode on the abdomen a wide angle of view can be used to search for a specific section of interest with the scanning device either hand held or connected to the scanning arm of a conventional B-scan unit. The rotation speed of the transducer head can be adjusted to optimize frame rate and line density while searching. Having found a section of interest the operator then has the choice of the two or four transducer mode to optimize angle of view or frame rate and line density. Alternatively using a single slow sweep of the ultrasonic beam the scanner can produce a high line density image of quality similar to that of a conventional B-scan unit.

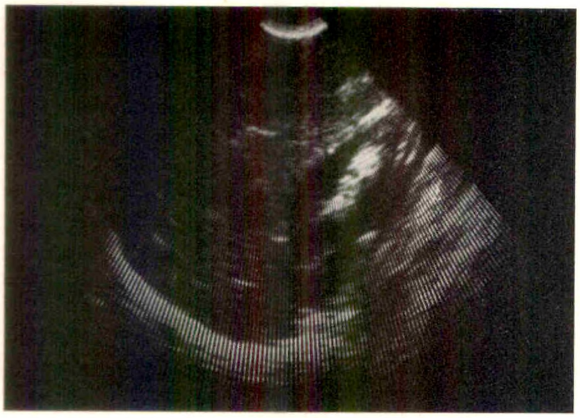

FIG. 5.

Longitudinal scan of upper abdomen showing liver and kidney.

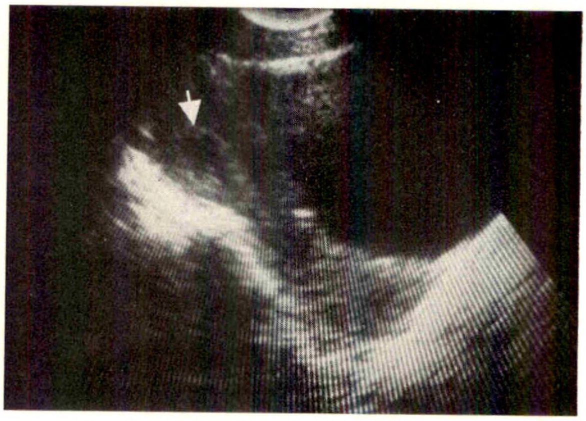

FIG. 6.

Early pregnancy. Arrow indicates gestation sac containing fetus.

A T-M trace can be generated from any one line in the section being imaged by gating this line out of every frame and brightness modulating a fibre optic chart recorder with the echo signals. The sampling rate (effective PRF) of this trace is that of the frame rate which can be increased having selected the line of interest in the section of high line density. Alternatively the scanner can be stopped with one transducer in a selected direction and a conventional T-M record made. This provides a high quality T-M record due to the high pulse repetition frequency and resolution of the ultrasonic signals.

Recording of real-time images can be achieved using a TV camera and video tape recorder. Instant playback of real-time images on a TV display is therefore possible and the recording material is re-usable. For cardiac work good quality still frames are required at specific parts of the cardiac cycle for quantitative analysis. A stop action facility which provides distortion free single frames is available on the more expensive TV systems. Real-time scan convertors also offer this facility and are being developed at present. A less expensive alternative is to use a cine camera synchronized with the scanner frame rate and to record every second ultrasonic frame. Alternate frames are not recorded during the cine film pull down time. The film is not instantly replayable but renders good quality still frames for analysis.

The mechanical scanner described makes use of standard transducers which can be driven by a conventional ultrasonic unit. Therefore when interfaced to such a unit it can be regarded as an accessory with obvious cost advantages over electronic scanners which require a unique electronic drive.

Due to its compact sealed design the scanner is suitable for visualization of the heart and abdomen as a hand held device. Figure 3 shows a longitudinal section of the heart which is a single frame from the series of successive frames illustrated in Fig. 4. A view of liver and kidney is shown in Fig. 5. In obstetrical applications maintenance of acoustic contact with the distended abdomen presents no problem due to the head size and therefore good large views are always possible. An example of a scan in early pregnancy is shown in Fig. 6.

A horizontal tubular version containing a similar sealed transducer head has been used to monitor fetal heart and breathing movements (McHugh *et al.*, 1978). This compact device can be strapped on to the abdomen once the appropriate section has been selected. A possible development of this format of device is to reduce its overall diameter and, using a single transducer head, achieve a 360° field of view for internal PPI scanning.

CONCLUSION

The rotating transducer scanner described has been successfully used in routine clinical applications. In initial trials 50 cardiac patients have been thoroughly examined. The device has also been used on approximately 300 obstetrics cases.

At present the large majority of real-time scanners commercially available are of the electronic type. The performance of the hand-held mechanical scanner described in this paper has been very acceptable in a range of clinical applications. This performance has resulted from the combination of the following design features. The use of modern standard transducers produces high resolution images and allows the device to be easily interfaced with conventional B-scan equipment. Rotation of the transducers in an oil filled chamber provides vibration-free coupling to the patient. The small size of the scanning head results in large fields of view from single points of entry on the skin surface.

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REFERENCES

BARBER, F. E., BAKER, D. W., STRANDNESS, JR., D. E., OFSTAD, J. M., and MAHLER, G. D., 1974. Duplex Scanner II: for simultaneous imaging of artery tissues and flow. *I.E.E.E. Ultrasonic Symposium Proceedings*, 744–748.

BOM, N., LANCEE, C. T., HONKOOP, J., and HUGENHOLTZ, P. G., 1971. Ultrasonic viewer for cross-sectional analysis of moving caridac structures. *Biomedical Engineering*, *6*, 500–508.

FLAHERTY, J. J., CLARK, J. W., and WALGREN, H. N., 1967. Simultaneous fluoroscopic and rapid scan ultrasonic imaging. Digest of the 7th International Conference on Medical and Biological Engineering, Stockholm, 321.

GRIFFITH, J. M. and HENRY, W. L., 1974. A sector scanner for real-time two-dimensional echocardiography. *Circulation*, *49*, 1147–1152.

HOLM, H. H., KRISTENSEN, J. K., PEDERSEN, J. F., HANCKE, S., and NORTHEVED, A., 1975. A new mechanical real-time ultrasonic scanner. *Ultrasound in Medicine and Biology*, *2*, 19–23.

KISSLO, J., VON RAMM, O. T., and THURSTONE, F. L., 1976. Cardiac imaging using a phased array ultrasound system. II. Clinical techniques and application. *Circulation*, *53*, 262–267.

MCDICKEN, W. N., BRUFF, K., and PATON, J., 1974. An ultrasonic instrument for rapid B-scanning of the heart. *Ultrasonics*, *12*, 269–272.

MCHUGH, R., MCDICKEN, W. N., BOW, C. R., ANDERSON, T., and BODDY, K., 1978. An ultrasonic pulsed Doppler instrument for monitoring humal fetal breathing in utero. *Ultrasound in Medicine and Biology*, *3*, 381–384.

SOMER, J. C., 1968. Electronic sector scanning for ultrasonic diagnosis. *Ultrasonics*, *6*, 153–159.

VON RAMM, O. T., and THURSTONE, F. L., 1976. Cardiac imaging using a phased array ultrasound system. I. System design. *Circulation*, *53*, 258–262.

1979, *British Journal of Radiology*, *52*, 34–35

Scintigraphic assessment of technetium 99m-diphosphonate uptake, vascularity and vessel permeability in human bone tumours

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ABSTRACT

Differences in the rate of uptake of ^{99}Tc^{m}-diphosphonate were found in 20 human bone tumours investigated. As some tumours have a slow rate of uptake it is suggested that the time used for routine scintigraphy at 3 hours is not always optimal and a further study should be performed in some cases. Various degrees of tumour vascularity and vessel permeability were found. The rate of diphosphonate uptake correlates with the vascularity, while it does not correlate with permeability which is generally increased as compared to normal bone.

Bone scintigraphy using ^{99}Tc^{m}-labelled phosphate complexes has achieved widespread use in diagnosis of bone lesions. It has been extensively used in detection of bone metastases. There are, however, few studies on the mechanisms involved in the uptake of bone-seeking agents. Most of them were performed *in vitro* or in animals—the model being bone fractures and rickets (Genant *et al.*, 1974; Garnett *et al.*, 1975; Siegal *et al.*, 1976). In the present study we have tried to assess the factors governing uptake of ^{99}Tc^{m}-diphosphonate in human bone tumours.

MATERIALS AND METHODS

Twenty patients with bone tumours detected by bone scintigraphy were investigated. Patients were studied using ^{99}Tc^{m}-diphosphonate for assessment of tumour uptake rate, ^{99}Tc^{m}-labelled red blood cells for tumour vascularity and ^{99}Tc^{m}-pertechnetate for tumour permeability (radiopharmaceuticals manufactured by Soreq Nuclear Research Center, Yavne, Israel). Labelled red blood cells were prepared from a commercial kit. *In vitro* and *in vivo* tagging efficiency of 97% is achieved using this kit. Strict quality control of free technetium was performed by chromatography before each study and by looking for uptake in the thyroid and parotid gland at the end of each study. The same protocol was followed in each case and with each of the radiopharmaceuticals. An early study followed the intravenous injection of 15 mCi of the radiopharmaceutical. Multiple views of the abnormal uptake were taken with an Anger-type gamma camera (Searle Pho Gamma IV), collecting 400000 counts for each view. This was followed by a similar study three hours later. Data were collected and processed by an Elscint data processing unit (CDP1-VDP2, Elscint, Haifa, Israel), as described by Garnett *et al.* (1975).

RESULTS

The results of the measurements are summarized in Table I. The rate of diphosphonate uptake R was defined as the ratio of late to early uptake.

$$R = \frac{\text{L/N late}}{\text{L/N early}}$$

(L/N = lesion to normal ratio)

Table I shows that the uptake ratios of lesion to normal in the early diphosphonate study were significantly higher than the uptake ratios of lesion to normal for labelled red-blood cells. The Man Whitney non-parametric test showed that the values of diphosphonate were stochastically larger than those for labelled red blood cells ($P = 0.001$). This indicates an early uptake of diphosphonate in the lesion. In cases 1–17 a higher rate of diphosphonate uptake is associated with high vascularity and vice versa. The Spearman rank correlation coefficient non-parametric test shows that the correlation between the rate of uptake and the lesion-to-normal ratio in red-blood cells is significantly negative ($P = 0.005$). When patients 18–20 are included it is less significant ($P = 0.05$). No correlation is found between the rate of uptake and blood vessel permeability studied by pertechnetate. The Spearman rank correlation coefficient non-parametric test shows that the correlation between lesion-to-normal ratio in pertechnetate and the rate of diphosphonate uptake is not significantly different from zero ($P > 0.10$).

DISCUSSION

The accumulation of diphosphonate in new bone is dependant on its uptake by newly-formed collagen (Wiegmann *et al.*, 1976) and hydroxyapatite crystals (Garnett *et al.*, 1975). Our results indicate that there is a marked difference in the rate of ^{99}Tc^{m}-diphosphonate uptake by bone tumours of different histological types and in different patients. The rate of

TABLE I

RATE OF DIPHOSPHONATE UPTAKE, TUMOUR VASCULARITY AND VESSEL PERMEABILITY IN 20 BONE TUMOURS

	Diphosphonate			Labelled red blood cells	Pertechnetate
Diagnosis	Early $\frac{\text{lesion}}{\text{normal}}$	Late $\frac{\text{lesion}}{\text{normal}}$	R $\frac{\text{late}}{\text{early}}$	$\frac{\text{lesion}}{\text{normal}}$	Early $\frac{\text{lesion}}{\text{normal}}$
(1) Metastatic follicular carcinoma of thyroid	2.58 ± 0.03	2.70 ± 0.05	1.09 ± 0.05	2.84 ± 0.05	2.90 ± 0.05
(2) Metastatic follicular carcinoma of thyroid	2.30 ± 0.08	2.84 ± 0.05	1.23 ± 0.04	1.90 ± 0.04	3.68 ± 0.15
(3) Metastatic breast carcinoma	4.16 ± 0.14	5.20 ± 0.12	1.25 ± 0.05	1.46 ± 0.03	1.41 ± 0.02
(4) Metastatic colon carcinoma	1.45 ± 0.06	2.00 ± 0.08	1.38 ± 0.08	1.05 ± 0.03	1.08 ± 0.04
(5) Metastatic carcinoma of stomach	2.16 ± 0.06	3.27 ± 0.09	1.46 ± 0.05	1.41 ± 0.04	1.22 ± 0.02
(6) Metastatic breast carcinoma	2.05 ± 0.04	3.14 ± 0.05	1.53 ± 0.04	1.35 ± 0.04	1.60 ± 0.03
(7) Metastatic hypernephroma	3.24 ± 0.08	5.25 ± 0.13	1.62 ± 0.06	1.00 ± 0.02	1.74 ± 0.03
(8) Metastatic breast carcinoma	2.16 ± 0.09	3.76 ± 0.17	1.74 ± 0.09	1.26 ± 0.03	2.27 ± 0.05
(9) Metastatic carcinoma of unknown origin	2.00 ± 0.06	4.70 ± 0.13	2.35 ± 0.09	1.21 ± 0.03	1.12 ± 0.03
(10) Metastatic breast carcinoma	3.64 ± 0.09	8.89 ± 0.32	2.44 ± 0.11	1.00 ± 0.02	2.13 ± 0.04
(11) Metastatic lung carcinoma	1.62 ± 0.05	4.00 ± 0.16	2.46 ± 0.12	1.03 ± 0.04	1.42 ± 0.05
(12) Metastatic breast carcinoma	1.58 ± 0.05	4.02 ± 0.09	2.54 ± 0.10	1.00 ± 0.03	1.05 ± 0.03
(13) Metastatic bladder carcinoma	1.72 ± 0.06	4.44 ± 0.16	2.58 ± 0.12	1.08 ± 0.04	1.66 ± 0.05
(14) Metastatic breast carcinoma	1.91 ± 0.04	5.14 ± 0.13	2.68 ± 0.09	1.08 ± 0.03	1.55 ± 0.04
(15) Bone involvement by cylindroma	1.42 ± 0.07	3.86 ± 0.11	2.70 ± 0.15	1.05 ± 0.03	1.21 ± 0.03
(16) Metastatic breast carcinoma	1.56 ± 0.03	4.65 ± 0.08	2.96 ± 0.08	1.04 ± 0.03	1.23 ± 0.02
(17) Metastatic breast carcinoma	1.00 ± 0.02	5.28 ± 0.23	5.28 ± 0.23	1.02 ± 0.02	1.12 ± 0.03
(18) Metastatic prostate carcinoma	2.34 ± 0.04	8.12 ± 0.18	3.47 ± 0.10	1.38 ± 0.03	2.42 ± 0.04
(19) Metastatic follicular carcinoma of thyroid	2.07 ± 0.04	8.30 ± 0.26	4.00 ± 0.15	1.41 ± 0.03	4.90 ± 0.12
(20) Basal cell carcinoma involving bone	3.00 ± 0.04	14.09 ± 0.20	4.69 ± 0.09	1.64 ± 0.03	3.81 ± 0.07

uptake may be slow in some tumours in which case the best time for scintigraphy may be later than the 3–4 hours used routinely. This explains the usefulness of 24 hour scintigraphy (Hardoff and Front, 1978). Uptake of ^{99}Tc^{m}-diphosphonate depends on its availability for the forming bone. Availability in turn is determined by the vascularity and permeability of the blood vessels supplying the tumour.

Vascularity varied in our cases; while in some it was not appreciably greater in the tumour than in the normal bone, in others it was markedly increased. Our results indicate that in cases 1–17 a rapid rate of diphosphonate uptake was associated with higher vascularity. Cases 18–20 behaved differently. They had an extremely high vessel permeability which is associated with early and continuous diphosphonate uptake. The result is a slow rate of uptake combined with high vascularity. Tumour vessels were markedly more permeable than those of normal bone, but there was no significant correlation between the rate of uptake and the degree of permeability.

CONCLUSION

Our data indicate that human metastatic bone tumours take up diphosphonate at different rates which are related to vascularity but not to vessel permeability. Tumour vessels are more permeable than those of normal bones.

REFERENCES

GENANT, H. K., BAUTOVICH, G. J., SINGH, M., LATHROP, K. A., and HARPER, P. V., 1974. Bone-seeking radionuclides: an *in vivo* study of factors affecting skeletal uptake. *Radiology, 113*, 373–382.

GARNETT, E. S., BOWEN, B. M., COATES, G., and NAHMIAS, C., 1975. An analysis of factors which influence the local accumulation of bone-seeking radiopharmaceuticals. *Investigative Radiology, 10*, 564–568.

HARDOFF, R., and FRONT, D., 1978. The value of delayed (24 hour) bone scintigraphy. *Clinical Nuclear Medicine*, (in press).

SIEGEL, B. A., DONOVAN, R. L., ALDERSON, P. O., and MACK, G. M., 1976. Skeletal uptake of ^{99}Tc^{m}-diphosphonate in relation to local bone blood flow. *Radiology, 120*, 121–123.

WIEGMANN, T., KIRSH, J., ROSENTHALL, L., and KAYE, M., 1976. Relationship between bone uptake of ^{99}Tc^{m}-pyrophosphate and hydroxyproline in blood and urine. *Journal of Nuclear Medicine, 17*, 711–714.

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An *in vivo* study of the fore-arm and hand by thin section NMR imaging

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ABSTRACT

A series of transverse thin section NMR images of the living fore-arm and hand is compared with the morphology of corresponding cadaver sections. Each image is derived from the distribution of the density of mobile protons within the section. The contrast and spatial resolution achieved indicate the potential information that future whole-body systems could provide.

In previous papers (Andrew *et al.*, 1977; Hinshaw *et al.*, 1978; Hinshaw *et al.*, 1977) we have shown high-definition, proton nuclear magnetic resonance (NMR) images of various objects up to 80 mm diameter obtained on our prototype 30 MHz NMR imaging system described in some detail in Hinshaw *et al.*, 1978. These were all thin section images consisting of a 128×128 array of picture elements.

Following the successful production of cross-sectional NMR images of the human wrist (Hinshaw *et al.*, 1977), we have now made a systematic study of the thin section anatomy of the fore-arm and hand by NMR. Our principal objective has been to try to indicate the likely potential of whole-body imaging systems currently under construction and this requires a preliminary discussion of the factors governing spatial resolution and contrast in the images.

There are grounds for expecting that NMR will be more than a mere alternative to conventional radiology and CAT scanning in displaying internal structure. Apart from its probable lack of hazard, it should prove possible to achieve a useful degree of tissue discrimination and characterization through analysis of components of the complex NMR signal.

PRINCIPLES

The principles of NMR imaging and of the multiple sensitive-point method used in this work were outlined in Hinshaw *et al.* (1978) and need not be repeated here. It is however worth emphasizing that the image is a map of the proton NMR response in the defined imaging plane, and that this is not a mere map of proton density.

At resonance the steady-state NMR signal from a volume element of a specimen, calculated from the Bloch equations (Hinshaw, 1976), is proportional to

$$M_0 \sin \alpha[(T_1/T_2+1)-(T_1/T_2-1)\cos \alpha]^{-1} \quad \ldots(1)$$

where M_0 is the equilibrium nuclear magnetization, α is the nutation angle of the radio frequency pulses and T_1, T_2 are the longitudinal and transverse relaxation times. Since M_0 is proportional to the number density ρ of protons at each point in the heterogeneous specimen, the NMR signal is everywhere proportional to ρ. The NMR signal is also dependent on the square bracket in (1), which is a function of the ratio (T_1/T_2).

If for illustration we take $\alpha = \pi/2$, expression (1) reduces to

$$M_0/[T_1/T_2+1] \quad \ldots\ldots\ldots\ldots(2)$$

For fluids and soft tissues, within which the molecules have a rate of molecular reorientation fast compared with the radio frequency, it is well-known that $T_1/T_2 \sim 1$, and expression (2) becomes $M_0/2$. If on the other hand the rate of molecular motion is slow compared with the radio frequency, as in solids and solid-like materials, $T_1/T_2 \gg 1$, and (2) reduces to $M_0(T_2/T_1)$. Thus the quantity in the square bracket in (1), or, more approximately, the ratio T_1/T_2, acts as a tissue contrast parameter, and adjacent tissues with the same proton density ρ but with differing (T_1/T_2) will appear with a markedly different NMR response in the image. Detailed information on the relaxation properties of components in the object may be obtained by varying α or by studying the dynamic response of the NMR signal.

Method used for the present work

The experiments were carried out using the apparatus previously described in Hinshaw *et al.*

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(1978) with the following parameters: field gradient strengths g_x, $g_z \simeq 0.2.10^{-4}$ T cm^{-1}, $g_y \simeq 1.5.10^{-4}$ T cm^{-1}, $\Omega \simeq 20$ Hz, pulse spacing = 2.5 ms, one line averaging time = 5 s. Image formation time for all images shown was therefore approximately ten minutes. The resonance phenomenon was excited and observed by a purpose-built 30 MHz spectrometer operating in the pulse Fourier transform mode. The final images consisted of 128 × 128 independent picture elements, and were displayed on a Hewlett Packard variable persistence oscilloscope. In the absence of any convention for the sense of the display of NMR images, we have here adopted the same convention as in Hinshaw *et al.* (1977) which is opposite to that chosen in Hinshaw *et al.* (1978). The reason for this choice (where high NMR signal appears black) was the relative ease of reproducing photographically a linear grey scale. The images on the oscilloscope screen were photographed onto Agfa Dia-Direct reversal film and printed on bromide paper, so that in the figures the highest NMR signal appears black. All the images were made with the above parameters, which were the optimum settings used for the particular wrist image shown in Hinshaw *et al.* (1977), although the resolution in some of the images could certainly have been improved by altering the settings.

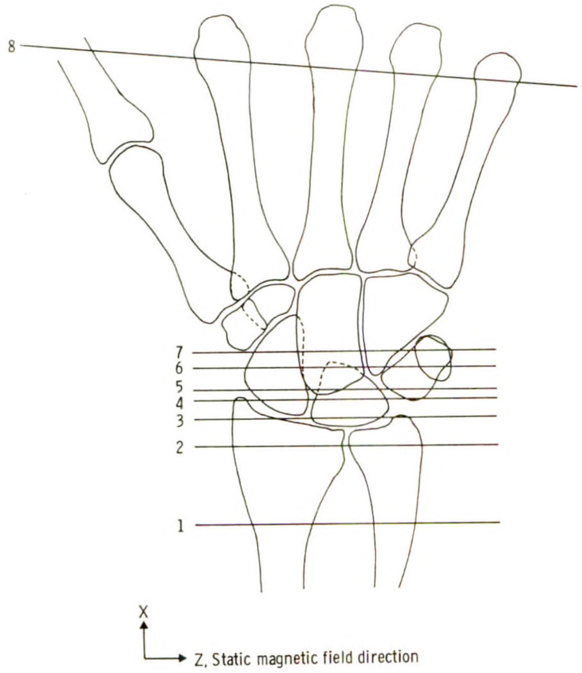
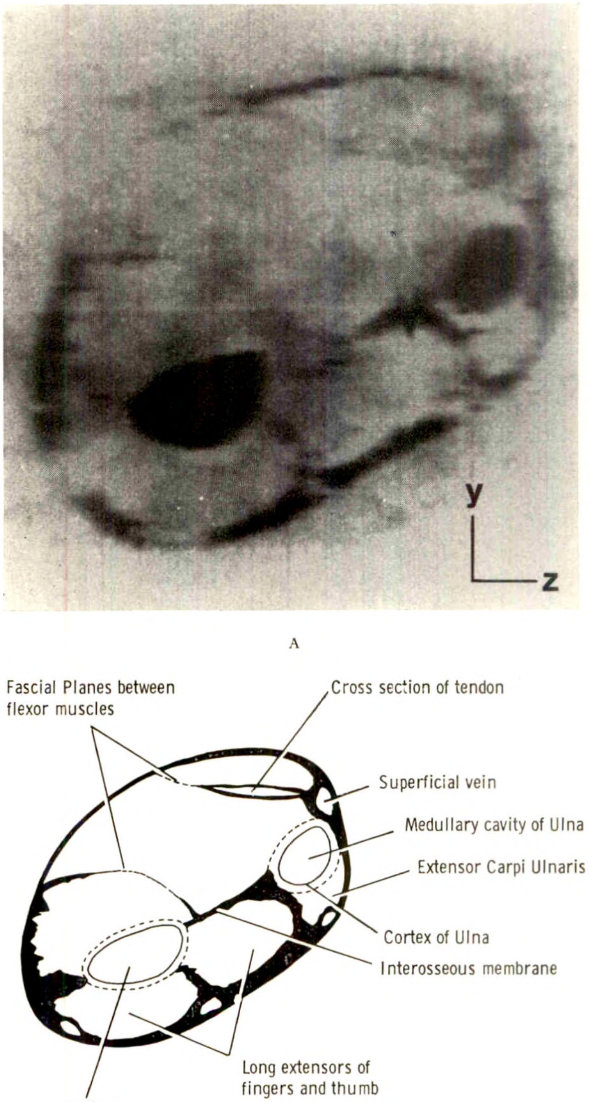


FIG. 1.
Level of transverse NMR sections related to the skeletal anatomy of the left fore-arm and hand.

RESULTS

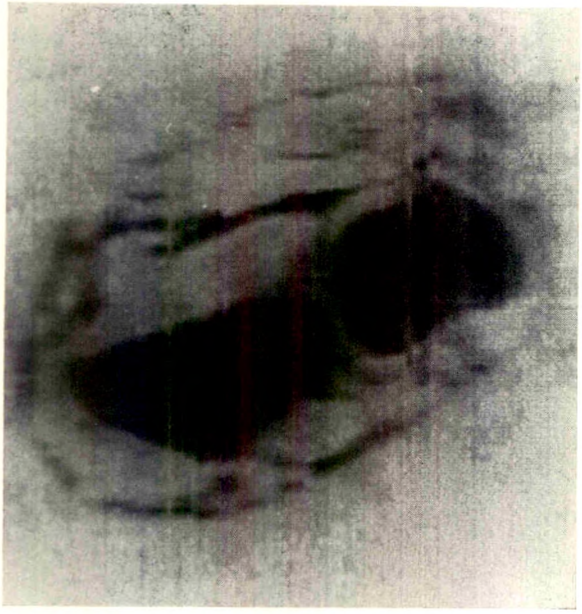
The lower left fore-arm and hand of one of the authors (GNH) was introduced into the sample chamber and a series of scans made in the yz or transverse plane. The posture of the wrist was largely determined by the chamber geometry. The exact position of the imaging plane relative to the wrist was difficult to determine because of the restricted space in the sample tube, and location of the sections was achieved indirectly as follows.



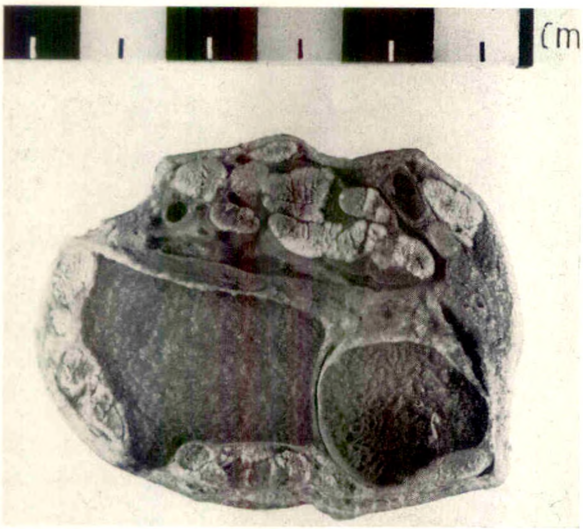
A

B

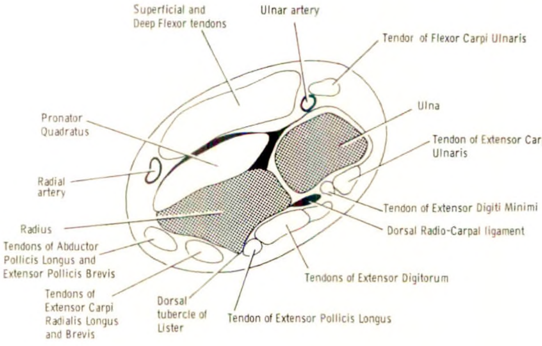
FIG. 2.
Section 1 through the lower fore-arm. (A) is the NMR image, (B) indicates the recognizable structure. (The y and z axes shown apply to all subsequent Figs.)



A



B


Superficial and Deep Flexor tendons
Ulnar artery
Tendor of Flexor Carpi Ulnaris
Ulna
Pronator Quadratus
Tendon of Extensor Carpi Ulnaris
Radial artery
Tendon of Extensor Digiti Minimi
Radius
Dorsal Radio-Carpal ligament
Tendons of Abductor Pollicis Longus and Extensor Pollicis Brevis
Tendons of Extensor Digitorum
Tendons of Extensor Carpi Radialis Longus and Brevis
Dorsal tubercle of Lister
Tendon of Extensor Pollicis Longus

C

Fig. 3.

Section 2 passing through the distal radio-ulnar joint. (A) is the NMR image and (B) the corresponding anatomical section. (C) indicates the recognizable structure.

An X ray was taken of a cadaver hand and forearm placed over a wire mesh grid. The position of the grid was related to the dorsal surface of the specimen by marking the position of its upper and lower borders with an indelible pencil. The NMR images were studied and an identification was made of the bones in each section. By referring back to the radiograph, a series of parallel lines was drawn to give a matching intersection of bony elements. Corresponding lines were then drawn on the surface of the specimen by relating their position to the reference grid, Fig. 1. After deep freezing the specimen overnight, transverse sections were made along the lines and each side of the resulting slices was then photographed. Although scans and anatomical sections derive from different individuals and a precise identification of the scan position was not possible, nevertheless, when the scans and anatomical sections were placed side by side, a very striking correspondence was seen which provided a confirmation of the accuracy of the initial identification of the bones within the sections.

Within the sections black areas correspond to regions containing a high density of mobile protons; these include the bone marrow within the carpal bones and connective tissues particularly if containing fat. The cortex of bone, articular cartilage and tendons have a very low density of mobile protons and appear white in the sections, while muscle and fibrous connective tissues have a granular appearance covering a tonal range of grey shades. The orientations of each section relative to Cartesian co-ordinates were known from the experimental arrangements and all were viewed as if looking along the positive x direction (Fig. 1), so that the radial aspect of the hand was on the left side. A number of structures are common to all the sections; of these the bones are the most obvious and easily identifiable; a rim of subcutaneous fascia forms a peripheral black band of variable thickness and numerous fascial planes are seen defining muscle bundles and forming an envelope in association with the flexor and extensor tendons. Many structures such as individual tendons and large blood vessels could be identified unequivocally because of their relationship

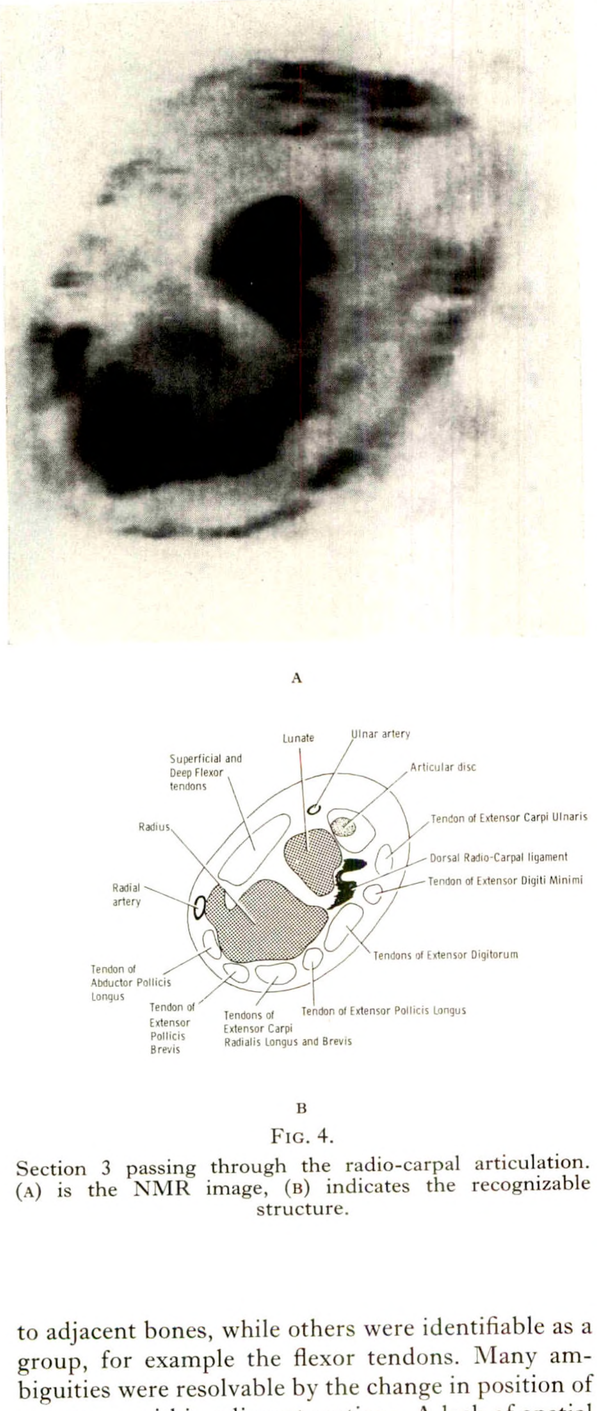

A
Lunate
Ulnar artery
Superficial and Deep Flexor tendons
Articular disc
Radius
Tendon of Extensor Carpi Ulnaris
Dorsal Radio-Carpal ligament
Radial artery
Tendon of Extensor Digiti Minimi
Tendons of Extensor Digitorum
Tendon of Abductor Pollicis Longus
Tendon of Extensor Pollicis Brevis
Tendons of Extensor Carpi Radialis Longus and Brevis
Tendon of Extensor Pollicis Longus
B

FIG. 4.

Section 3 passing through the radio-carpal articulation. (A) is the NMR image, (B) indicates the recognizable structure.

to adjacent bones, while others were identifiable as a group, for example the flexor tendons. Many ambiguities were resolvable by the change in position of structures within adjacent sections. A lack of spatial resolution in some sections resulted in a failure to delineate known structures.

Figure 2 is the most proximal section and passes through the lower forearm. The radius and ulna both show a homogeneous central black area corresponding to marrow within the medullary cavity which is surrounded by a thin white halo representing cortical bone. The interosseous membrane joins the medial border of the radial shaft to the lateral border of the ulnar shaft. Several fascial planes are delineated which separate muscle groups in the flexor and extensor compartments of the fore-arm. Within the black band of subcutaneous fascia several well-defined white elliptical areas are seen which represent superficial veins.

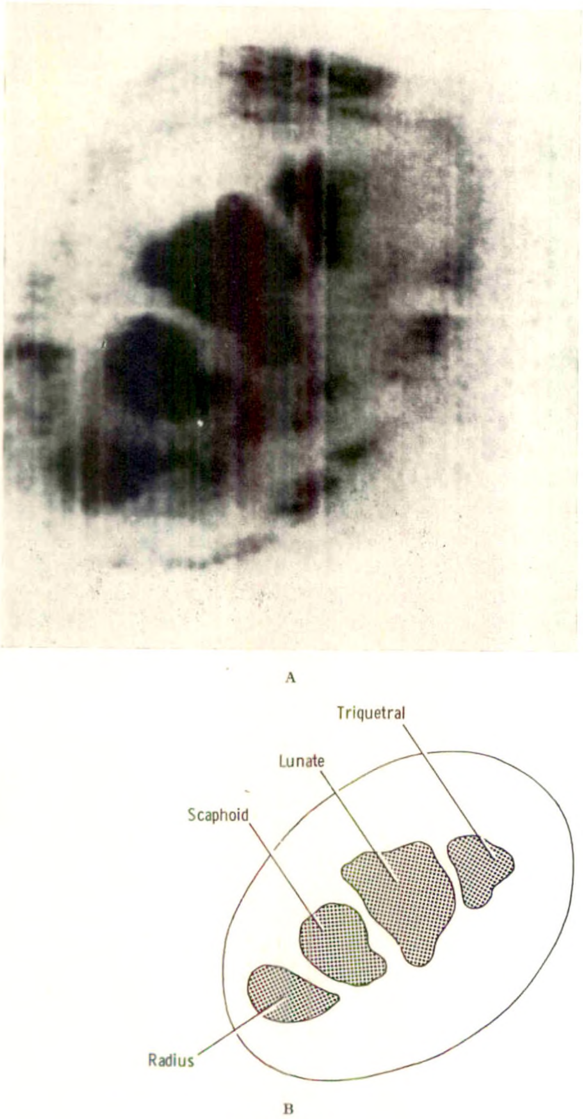
Figure 3 is a section through the distal radio-ulnar joint. The cross-section of the radius and ulna are seen centrally within the section and around the periphery is a rim of subcutaneous fascia. The lower end of the radius shows, on its medial side, a shallow concave border for articulation with the ulna. Adjacent to its anterior surface is the belly of the pronator quadratus muscle surrounded by a well-defined fascial envelope. The posterior surface extends from the posterior border of the ulnar notch to the prominent subcutaneous dorsal tubercle of Lister. Immediately medial to the groove is the tendon of extensor pollicis longus and contiguous to it the tendons of extensor digitorum. Adjacent to the lateral surface which extends from the tubercle to the lateral border of the anterior surface are, from before backwards, the tendon of abductor pollicis longus and extensor pollicis longus in a common synovial sheath, and the sheath containing the tendons of extensor carpi radialis longus and brevis, adjacent to the root of the styloid process. The dorsal radio-carpal ligament is seen as a short dark band arising from the posterior surface of the radius beneath the tendon sheath of extensor digitorum.

The inferior end or head of the ulna has, on the anterior and lateral parts, an articular circumference for the ulnar notch of the radius. The base of the styloid process lies laterally; medial to it is a shallow groove for transmission of the tendon of the extensor carpi ulnaris and immediately adjacent is the small tendon sheath of the extensor digiti minimi.

The superficial and deep flexor tendons are not individually resolved, but several fascial planes associated with their sheaths are seen. The radial and ulnar arteries appear as ring shadows, the former adjacent to the lateral border of pronator quadratus and the latter adjacent to the tendon of flexor carpi ulnaris.

Figure 4 is a more distal section passing through the radio-carpal articulation. Here the ulna has been replaced by the lunate and an articular disc of fibro-cartilage while the tendons and their disposition are little different from the previous section. There is an area of reduced density on the medial half of the radius because this border is concave and its cross-section has, therefore, a substantial component of articular cartilage which reduces the total NMR signal.

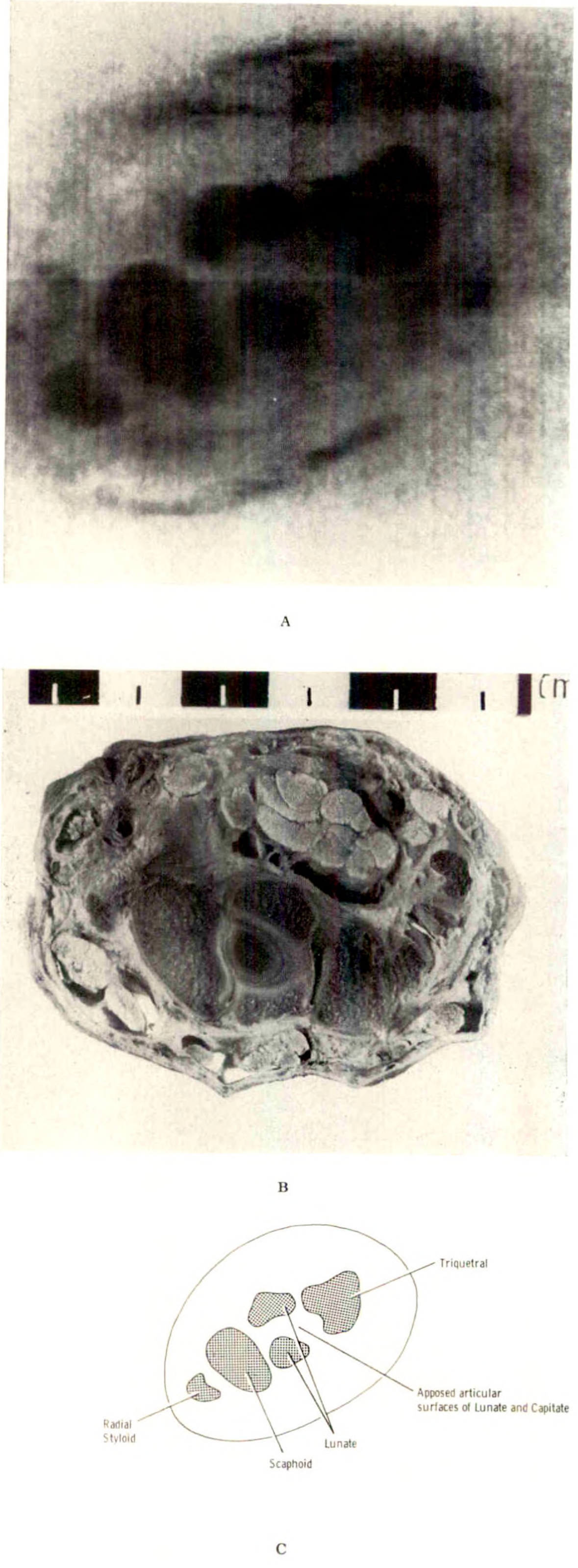
Figures 5 and 6 are two closely adjacent sections through the proximal carpus. From lateral to medial



A

B

FIG. 5.
Section 4 passing through the proximal carpus. (A) is the NMR image, (B) indicates the recognizable structure.



A

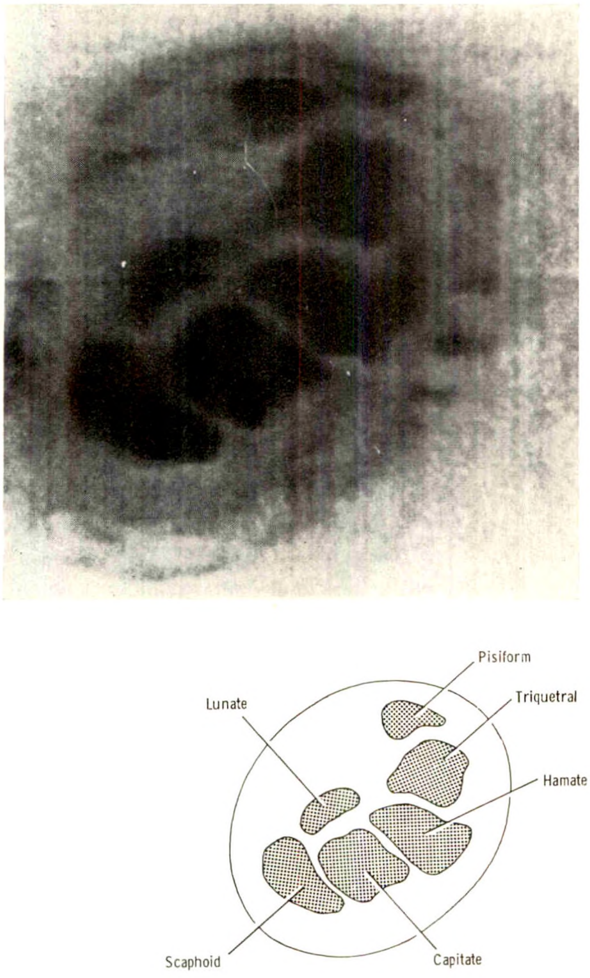
B

C

FIG. 6.
Section 5 more distal plane passing through the proximal carpus. (A) is the NMR image and (B) the corresponding anatomical section. (C) indicates the recognizable structure.

the bones in each are the styloid process of the radius, the scaphoid, the lunate and the triquetral.

Figure 6 is the more distal segment. The tapering styloid process is correspondingly smaller while the scaphoid and triquetral are larger in cross-section. This section passes through the articulation of the capitate with the lunate and the contiguous articular surfaces of cortical bones and cartilage produce a dark transverse cleft in the lunate.



B

FIG. 7.

Section 6 passing through the mid-carpus. (A) is the NMR image, (B) indicates the recognizable structure.

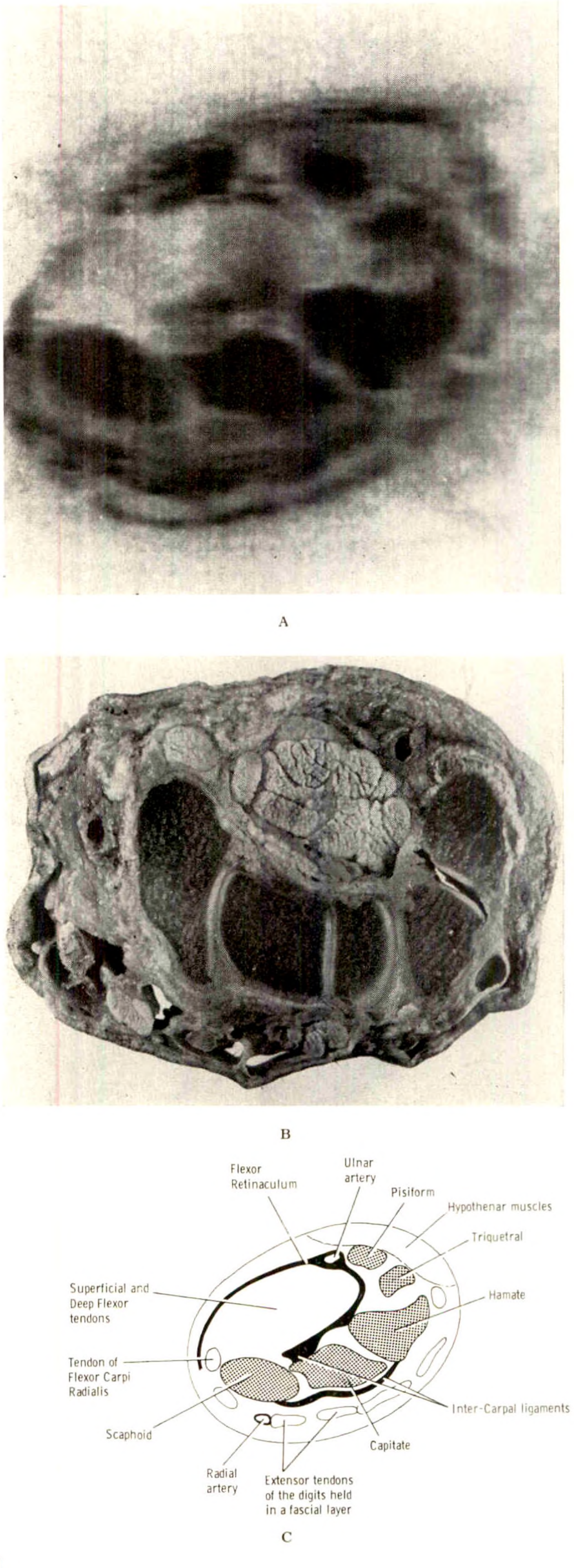


FIG. 8.

Section 7 passing through the proximal end of the carpal tunnel. (A) is the NMR image and (B) the corresponding anatomical section. (C) indicates the recognizable structure.

Figures 7 and 8 are closely adjacent sections through the mid-carpus and the proximal end of the carpal tunnel. In Fig. 7, which is the more proximal, the carpal elements are, from lateral to medial, the scaphoid, the capitate, the hamate and the triquetral surmounted by the pisiform. Anterior to the capitate, separated by a dark cleft of contiguous articular surfaces, is part of the lunate.

Figure 8 shows the hamate to have a greater cross-section and the triquetral and pisiform to be smaller. The fibrous flexor retinaculum is seen extending from the pisiform to the tubercle of the scaphoid. Beneath it is an elliptical tunnel transmitting the flexor tendons whose floor is formed by several inter-carpal ligaments. The individual flexor tendons within the tunnel are not resolved. Anteriorly and medially is the hypothenar space containing the ulnar artery and the hypothenar muscles which appear as a granular density adjacent to the pisiform and triquetral bones. The extensor tendons of the digits and thumb are held in a fascial layer and these can be seen on the dorsal aspect of the carpus. The radial artery appears as a ring shadow adjacent to the scaphoid bone.

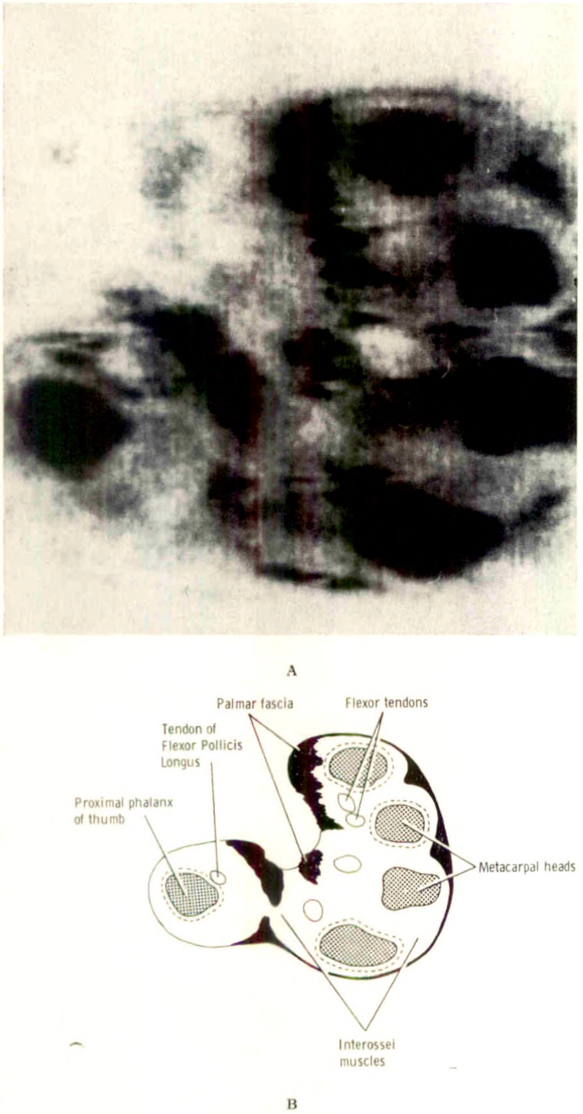


FIG. 9.

Section 8 passing through the mid-hand with the thumb held in adduction. (A) is the NMR image and (B) indicates the recognizable structure.

Figure 9 is a section through the mid-hand with the thumb held in adduction. This passes through the heads of the metacarpals and the proximal phalanx of the thumb and also intersects the subcutaneous tissue covering the first interspace. The thick layer of palmar fascia is outlined and the corrugations of the palm, produced by circumferential compression of the hand within the narrow sample chamber, are clearly seen. The principal flexor tendons appear as light areas close to their respective digits (cf finger images, Mansfield and Maudsley, 1977).

DISCUSSION

As with CAT scanning, resolution of soft tissue detail is at a premium in NMR imaging. The in-plane resolution in the y and z directions is excellent as can be gauged from the anatomical detail identifiable in section 2 (Fig. 3).

Sections 4 and 5 (Figs. 5 and 6) are the closest together and from a consideration of the cross-sectional anatomy of the carpal bones when referred back to the cadaver sections and radiograph it can be estimated that these are separated by approximately 5 mm. The thickness of the imaging plane is thus clearly less than 5 mm.

In our present study transverse sections were chosen but sagittal and coronal planes are no more difficult to image by NMR and the equipment could be designed to image any plane in any orientation. The contrast exhibited in the images is consistent with equation 1 in that the highly mobile protons in marrow and fascial tissue give the largest signals, whereas the more solid-like cartilages and tendons give the lowest signals, although it is difficult to make quantitative measurements. As explained earlier, the contrast can be altered by variation of the image collection parameters and an imaging window level can be chosen by subsequent computer processing.

The absence of the expected high signal from blood within the arteries is due to its continued motion into and out of the imaging plane which reduces its NMR signal considerably, since the equilibrium steady-state signal is never obtained. This offers a potential method of *in vivo* measurement of blood flow. The light lines crossing some of the images vertically (Figs. 3 and 5) are also due to motion, in that if the wrist moves during the averaging period for one particular line of the image, the signal is again reduced because of the time required to attain the steady-state response. It therefore seems that in future whole-body images, high signals will be obtained from marrow, fascial tissue, and stationary blood pools, and that depending on flow rate the signals from arterial and venous blood will range down to zero but will nevertheless allow differentiation of the cross-section of large regions of flow by the signals from surrounding tissue. It should be noted that in whole-body images the minimum resolvable features will have dimensions approximately given by (image diameter)/128, assuming that the number of picture elements in the image remains the same. This is because of the rapid variation in time to acquire the image versus the array size for a given signal-to-noise ratio. The averaging time for a line of the image depends on the volume of the sensitive line and the resolution required along the line, which will normally be the same as the line "thickness" for equal z and y resolution.

NMR relaxation times in normal and pathological tissue have received considerable attention in the literature (see Hinshaw *et al.*, 1978) and are being studied in this laboratory. The differing relaxation times should aid in the discrimination between the normal and the pathological, but the work to date shows an overlap in the values suggesting that relaxation times alone are insufficient. Further work is required to find the best discriminants which NMR parameters can provide with the ultimate objectives of tissue characterization. It is noteworthy that previous work has been carried out on excised tissue and the situation may well be different in living tissue.

The sections produced in this study were based upon the resonance of protons, but other nuclei could be chosen. The ^{19}F nucleus, for example, gives a strong signal and images based on the resonance of the fluorine nucleus have recently been published from this laboratory (Holland *et al.*, 1977). The introduction of fluorine-containing compounds into the circulation would enable the vascular bed of body organs to be studied without interference from surrounding tissues and this would be analogous to blood-pool assessment by radioactive isotopes.

The hazard associated with our procedure has already been discussed briefly by Hinshaw *et al.*, (1978); there are three distinct possible causes, namely the static magnetic field, the radio frequency pulses and the time-dependent gradients. Static fields of 0.1 T which will be used in whole-body imaging systems seem unlikely to be hazardous (Barnothy, 1964; 1969). The RF volume power dissipation has been calculated (Bottomley and Andrew, 1978) to be less than 1 mW cm^{-3}, which corresponds to a flux density of less than 10 mW cm^{-2} (Schwan, 1972) for our projected full-body system operating below 5 MHz. This level is below the recommended maximum safe working level for non-ionizing radiation (Min. Tech., 1968). Finally, the time-dependent gradients cause negligible heating, although the Faraday-induced voltages in conducting loops within the body could become appreciable in other systems where the gradients are changed very rapidly.

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We would also like to thank Professor R. Coupland for the use of facilities in his Department, Mr. F. Young for the preparation of the cadaver sections, Miss C. Simaroj for her capable assistance with computer programming, and Mr. A. Bezear for the illustrations.

REFERENCES

ANDREW, E. R., BOTTOMLEY, P. A., HINSHAW, W. S., HOLLAND, G. N., MOORE, W. S., and SIMAROJ, C., 1977. NMR images by the multiple sensitive point method: application to larger biological systems. *Physics in Medicine and Biology*, *22*, 971–974.

BARNOTHY, M. F., Editor, *Biologic effects of magnetic fields*, (Plenum Press, New York) Vol. 1, 1964, Vol 2, 1969.

BOTTOMLEY, P. A., and ANDREW, E. R., 1978. RF magnetic field penetration, phase shift and power dissipation in biological tissues: Implications for NMR imaging. *Physics in Medicine and Biology*, *23*, 630–643.

HINSHAW, W. S., 1976. Image formation by nuclear magnetic resonance: the sensitive point method. *Journal of Applied Physics*, *47*, 3709–3721.

HINSHAW, W. S., BOTTOMLEY, P. A., and HOLLAND, G. N., 1977. Radiographic thin-section image of the human wrist by nuclear magnetic resonance. *Nature*, *270*, 722–723.

HINSHAW, W. S., ANDREW, E. R., BOTTOMLEY, P. A., HOLLAND, G. N., MOORE, W. S., and WORTHINGTON, B. S., 1978. Display of cross-sectional anatomy by nuclear magnetic resonance imaging. *British Journal of Radiology*, *51*, 273–280.

HOLLAND, G. N., BOTTOMLEY, P. A., and HINSHAW, W. S., 1977. ^{19}F magnetic resonance imaging. *Journal of Magnetic Resonance*, *28*, 133–136.

MANSFIELD, P. and MAUDSLEY, A. A., 1977. Medical imaging by NMR. *British Journal of Radiology*, *50*, 188–194.

MINISTRY OF TECHNOLOGY, 1968. *Intense radiofrequency radiation code of practice*, Report BR 19945.

SCHWAN, H. P., 1972. Microwave radiation: biophysical considerations and standards criteria. *IEEE Transactions on Biomedical Engineering*, *BME-19*, 304–312.

1979, *British Journal of Radiology*, 52, 44–50

A calibration system for X-ray generators and tube factors

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ABSTRACT

An apparatus (Machlett's Dynalyzer II system) is described that makes real-time dynamic tests on the output and performance of the X-ray tube and generator so that a single exposure gives information on mA and mAs; exposure time (ms); kVp anode to earth; kVp cathode to earth; kVp cathode to anode; tube filament current; line voltage and radiation output of the tube (mR). The method of use is described together with the results of comparisons made with other test equipment. Some novel design features are of particular interest. The results show that by using this apparatus present design characteristics of X-ray generator-control-tube systems are such that the accuracy of calibration can be improved by at least an order of magnitude.

All progress in diagnostic radiography since 1895 has been toward increasing the dependence of the radiographer on the apparatus producing the primary beam. For instance, exposures are measured in milliseconds rather than minutes and radiographers are expected to carry out many different examination techniques using several types of apparatus, often by more than one manufacturer, usually in a department containing several diagnostic rooms. In order that consistent results can be obtained under these conditions, the radiographer must be reasonably confident that exposure factors that apply with one machine can be used with another, or indeed with all machines. This is an ideal condition that too often is not achieved in practice, yet there is usually little the radiographer can do other than increase or decrease the exposure in accordance with his experience and to report the apparent defect to his superintendent.

A physicist experienced in diagnostic radiology could help with these problems, but at present such physicists are relatively uncommon in the United Kingdom. In the absence of such an expert, the superintendent or the hospital physicist should have access to a dosemeter and/or a cathode-ray oscilloscope, but even if the manufacturers' engineers are called in there is comparatively little they can ordinarily find out about the output of the generator and the X-ray output of the tube without going to a great deal of trouble that would take the set out of commission for a relatively long period.

Problems can also arise when we consider what is being measured. For instance, an Ardran-Crookes penetrameter cassette measures effective kilovoltage by the radiation produced. A potential divider system measures peak kilovoltage and a cathode-ray oscilloscope shows the waveform. All these measure different aspects of tube performance and some compromise may be needed between the users and the testers as to which standard should be applied in a particular case.

A system is now available that makes real-time dynamic tests possible on the output and performance of the X-ray tube and generator, either separately or together. The apparatus is the Dynalyzer II from Machlett X Ray Tubes (Great Britain) Ltd. It is inserted in the secondary side of the high voltage circuit between the high tension generator and the X-ray tube (Fig. 1), and a single exposure can give all the following information: mA and mAs; exposure time (ms); kVp anode to earth; kVp cathode to earth; kVp cathode to anode; tube filament current; line voltage; radiation output of the tube (mR).

A paper-tape printer is included in the Dynalyzer system, so that an intermittent fault can be investigated by leaving the apparatus in circuit all day, so that each exposure is logged for off-line analysis.

DESCRIPTION OF APPARATUS

The high voltage unit (Figs. 1 and 2) encloses a high-voltage divider network, an anode current sensor and a filament current monitor. The high-voltage divider inserts 1000 megohm resistances between the anode and earth and the cathode and earth, the rated anode-cathode voltage being 150 kVp. The voltage is measured across a 10000:1 step-down section with ±1% accuracy.

The anode current sensor is an optically-coupled device to give a signal that represents the anode waveform. Currents from 1 mA to 2 A can be measured with a claimed accuracy of ±4% for currents less than 10 mA and ±2% for currents over 10 mA. The output conversion factor is 1 mV per mA of anode current and this output voltage is electronically buffered so that it can be coupled to a cathode ray oscilloscope or other measuring device.

The means of producing an isolated input that represents the anode current is an innovation. The anode current is sampled through a 1 ohm resistance. The signal is amplified and then fed to a gallium

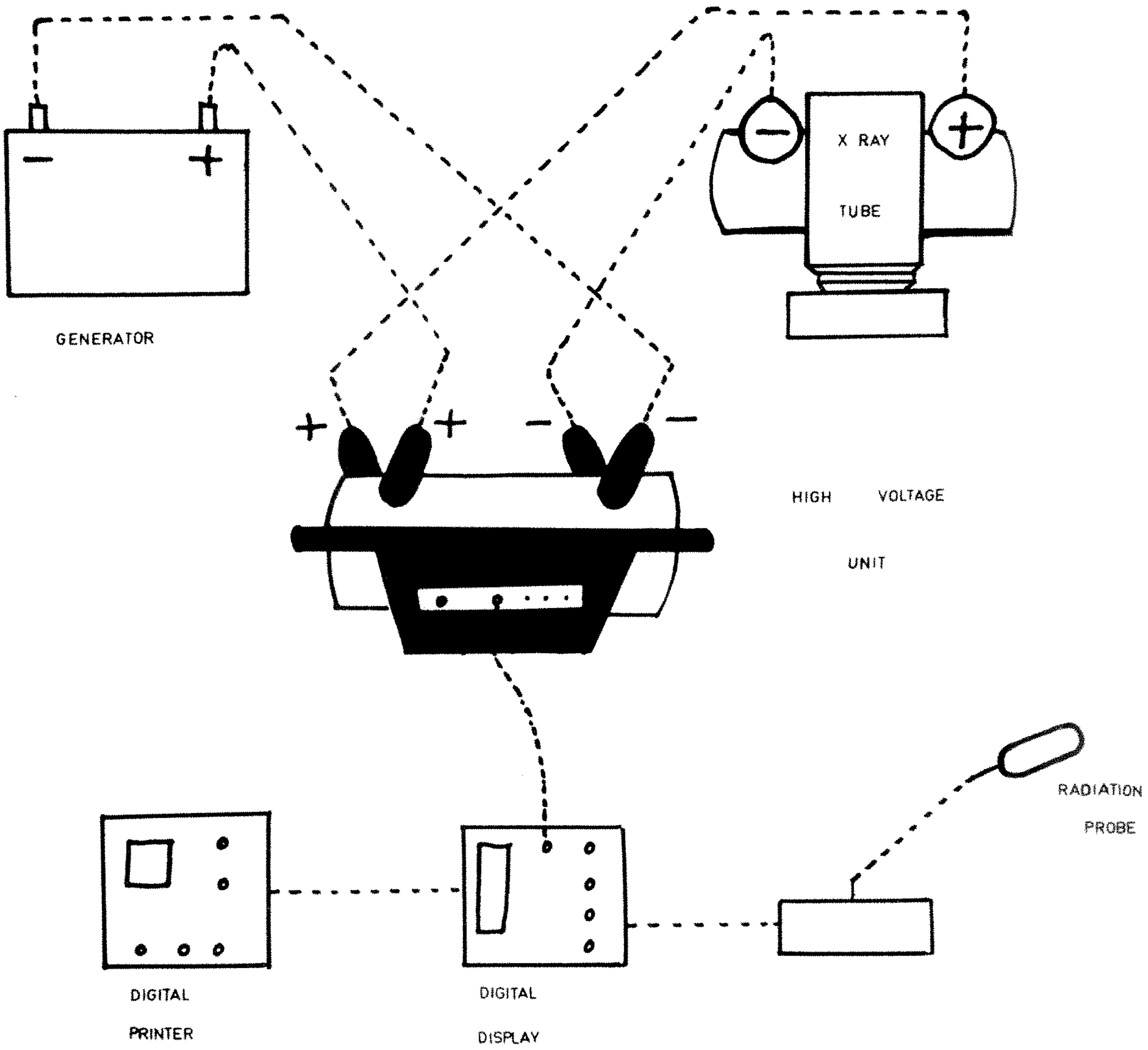


FIG. 1.

Block diagram to show how the Dynalyzer II system is incorporated in the high tension circuit.

arsenide infra-red light-emitting diode. The light signal from this device is proportional to the current sampled. It is optically coupled through a glass light-pipe to a photodiode. The output from this diode is again amplified and then fed to the display unit.

The tube-filament current monitor uses an isolating toroidal transformer in the common lead of the filament circuit. It can measure currents up to 20 A. Claimed accuracy is ±1% at 50 Hz.

The digital display unit (Figs. 1 and 3A) and the paper-tape printer (Figs. 1 and 3B) are part of the Dynalyzer II system. For fullest utilization of the equipment, a dual-trace cathode-ray oscilloscope and a radiation probe are needed in addition. Any cathode-ray oscilloscope can be used, but the impedance of the output of the ionization chamber needs to be matched to that of the digital display unit. The output of the high-voltage unit is frequency compensated for cable length, high voltage transients and for oscilloscope impedance factors, so that the overall accuracy of the voltage readings on the cathode-ray oscilloscope is normally limited by the accuracy of the oscilloscope used. The accuracy of the digital display unit is usually at least an order of magnitude higher.

Method of connection

The secondary circuit of the high tension supply to the X-ray tube is interrupted by removing the high voltage cables from the tube and connecting them into the Dynalyzer II high-voltage unit (Fig. 1). Jumper cables are then used to connect the high-voltage unit to the tube. A direct connection is then made from the high-voltage unit to the digital display unit, by means of a multi-core cable, and thence to the digital printer. A 240 V supply is taken to the three components of the Dynalyzer II system from a common point. This is to prevent any earth loop becoming established. The oscilloscope takes its electrical supply from the same mains and connections are then made to the appropriate sockets on the digital display unit so as to view the anode and cathode wave forms. Another socket accepts the lead from the radiation probe.

Method of operation

The high-voltage waveform is unlikely to be identical from set to set, so that there is a need to select the most useful point on the waveform. This point at which readings are to be taken can be affected in four ways. Firstly, a built-in delay can be switched out when making exposures of less than 3 ms. Secondly, there is a vernier scale to select the triggering point. For single phase units, a point at 10% of the peak is advised, and for 3-phase units a point at 75% of the peak. It is also possible to include an additional delay of up to 20 ms before kVp measurements are made and finally triggering can be either external or, if internal, from the kV or mA wave forms.

In practice, it was found that an initial 10 ms delay was essential to prevent the apparatus recording the initial spike on any exposure. With regard to the vernier settings, the recommended levels of 10% for single phase and 75% for 3-phase were found to be a good general guide. We did find on some occasions, however, output waveforms that necessitated measurements being taken at the 50% point.

Method of Testing

During the evaluation of the apparatus, exposures were made utilizing all the variables and noting the effects on the indicated factors. For each set of conditions on the Dynalyzer II system (*e.g.* automatic

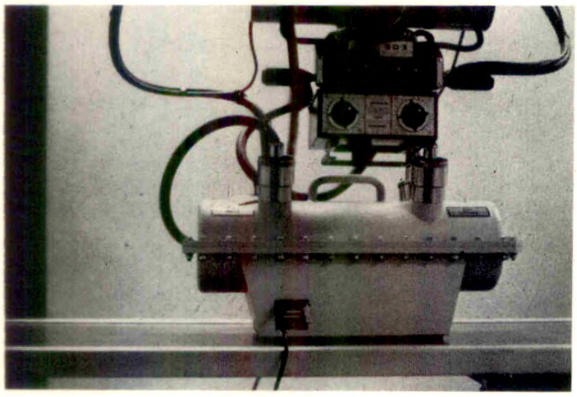
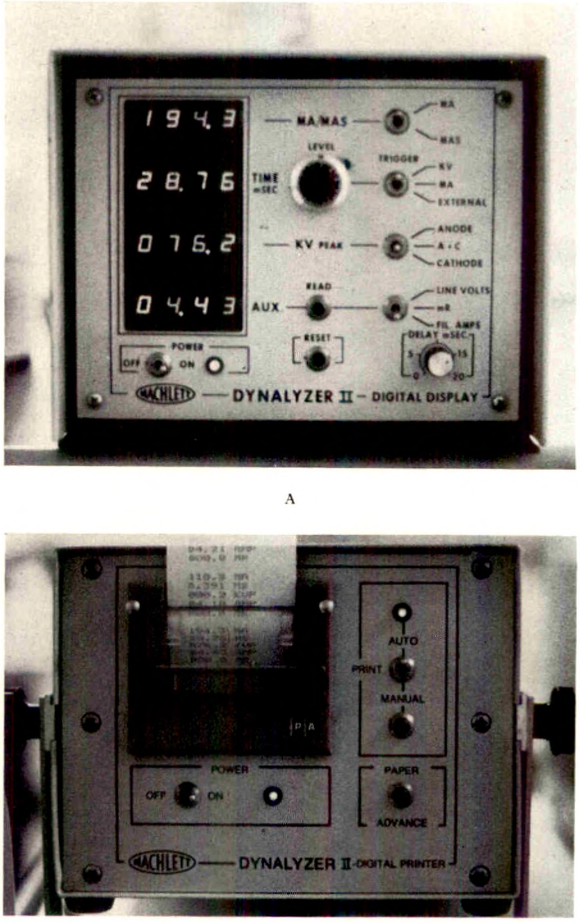


Fig. 2.
The high voltage unit containing a high voltage divider, an anode current sensor and a filament current monitor.



A

B

Fig. 3.
(A) The digital display unit and (B) the paper tape printer of the Dynalyzer II system.

delay "ON", 10% of waveform, kV trigger, 10 ms delay) tests were made as shown in Table I. When each set of tests had been carried out, the whole procedure was repeated with a different set of conditions being selected on the Dynalyzer II.

When these results were being obtained, some additional constraints became apparent. Firstly, it was found that the extra cable in the high tension circuit imposed such a load on the X-ray system that the tube current was significantly lowered, with an accompanying drop in kVp—contrary to what might have been expected. Allowance must be made for this in any calibration of settings on the control panel.

It was found that the Dynalyzer II is much more sensitive to variations in the line voltage than is the usual "automatic" compensator on the X-ray apparatus. This meant that a given stud setting

TABLE I

	kVp		mA		Time		mAs	
	Constant	Varying	Constant	Varying	Constant	Varying	Constant	Varying
mA check	√			√	√			√
mAs check	√			√		√	√	
kV check		√	√		√		√	
Timer check	√		√			√		√
Repeatability check	√		√		√		√	

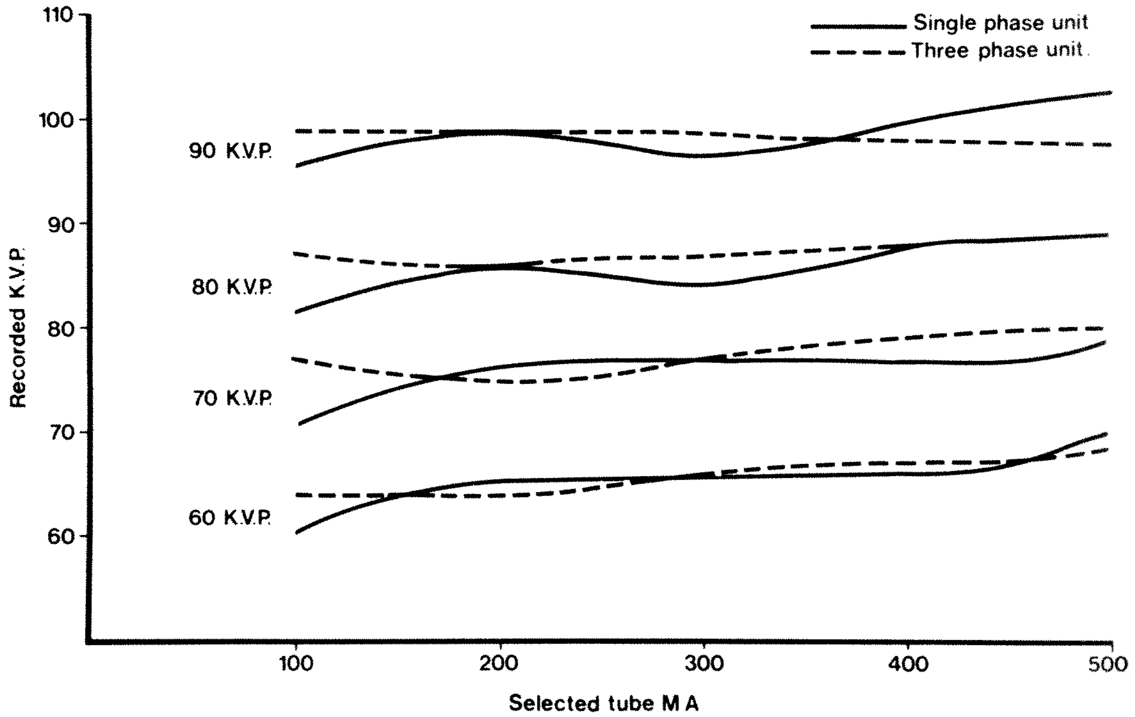


FIG. 4.

Typical results obtained with the Dynalyzer II system showing the variation in actual kVp output against tube mA for various selected values of kVp.

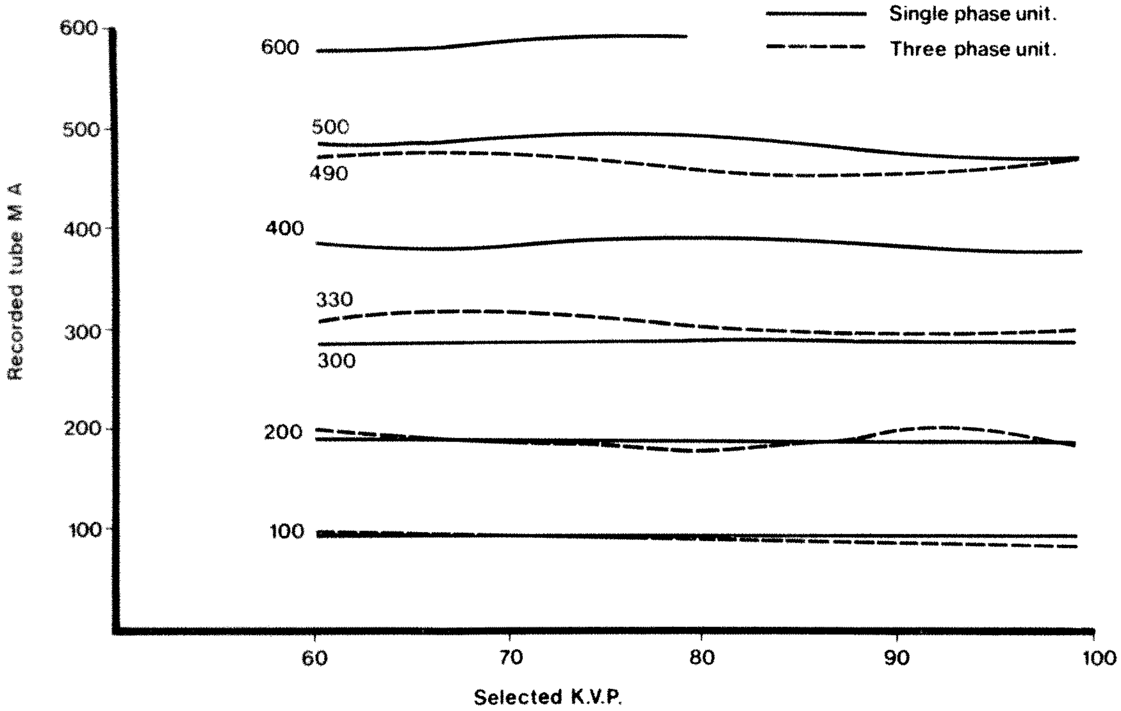


FIG. 5.

Variation in actual generated mA against the selected kVp for chosen mA values. These are the same X-ray units as were tested to give Fig. 4.

might give a different high-voltage output at different times, due to these variations in the line voltage. This is no fault in the Dynalyzer II system, for it accurately follows these changes, but it does mean that accurate calibration of the control settings can be impossible if the mains voltage is significantly variable. When the kVp and time are kept constant and a series of readings is taken with variation in the mA used, then, in general, as the mA increases the kVp would drop. The apparatus is arranged so as to compensate for this effect but, if the mains voltage is also varying, the compensation may not be exactly proportional to the change in mA. A change of ±5% in the actual kVp has frequently been detected in Barnsley, where the mains supply is particularly erratic. Although such a change would probably not be detected on the film, this effect must be remembered whenever the Dynalyzer II is used to check or calibrate stud settings.

It was also found that although it is remarkably easy to make deductions as to the shape of the waveform even without a cathode-ray oscilloscope, in practice it is a great advantage to know the shape of the kVp output waveform before undertaking a test exposure. This is in order to determine what delay should be applied before the reading-point and to decide at which point to start the measurement of exposure time.

RESULTS

It would be impracticable to list all the results here. Even from one generator and one tube an enormous quantity of data becomes available. Our aim was to assess the Dynalyzer II system rather than the X-ray apparatus, so that we tested many installations and checked wherever possible against other measuring devices. In most of the tests, the equipment suppliers and their engineers gave full co-operation and these units were tested concurrently with their own test equipment. There were a few instances where the X-ray equipment suppliers and we have agreed to differ over slight differences of calibration, but such differences have been minor, especially when the width and intensity of the oscilloscope trace is taken into account. We were fortunate in being able to assess the Dynalyzer II on new equipment being installed in a new department by all four major suppliers, as well as in several older departments containing well-used apparatus.

An example of the type of result obtained when making measurements on single- and 3-phase units is shown in Fig. 4. When this type of curve was first obtained, at first sight it seemed that the units under test were poorly aligned, but closer examination of the tube current results suggested that the tube mA was low and that this was giving rise to the unexpectedly high kVp. The tube mA values for these units are shown in Fig. 5, wherein it will be seen that the mA did not vary with selected kVp in the way that the recorded kVp varied with selected tube current. Eventually, the explanation was found to lie in variations in line voltage and the sensitivity of the Dynalyzer II to these variations mentioned above.

In summary, our findings were:

mA check	gives an average reduction of 8% in mA with constant kVp, when both HT cables were connected. The variations between the readings was <1%.
kV check	With both HT cables inserted, the reduction in mA gave a rise in kVp of 8–10%.
Timer check	The variation between readings was <1% using kV trigger, average variation 3.2% using mA trigger, average variation 1%.
Repeatability check	<1% variation.

When the cathode cable was disconnected from the high-voltage unit and reconnected directly to the X-ray tube, the load on the cathode circuit was removed, and the mA results were accurate to within 1%. Consequently, the indicated kVp rose to the level needed to compensate this effect.

The maximum variation between results was found to be 1.15%, both on testing different tube-generator systems and repeated tests on one apparatus.

DISCUSSION

The Dynalyzer II test system is a very sensitive apparatus that gives excellent reproducibility and consistent results. It can be used in two ways, both during the initial calibration and alignment of the X-ray generator-control-tube system and as a running check on the system's performance throughout its working life. The Dynalyzer II is so sensitive that the user must be aware of the limitations of the X-ray equipment that is being tested, because it is very easy to misinterpret the results obtained and to ascribe a permitted variation to an apparatus fault. In most instances, a view of the output waveform is essential.

Another finding was that when tests were being made on apparatus that had been aligned in the conventional manner by the supplier's engineers, the load presented by the Dynalyzer II unit was not acceptable and it was found that it was better to operate with only the anode cable connected into the circuit when measuring mA and kVp. This necessitated that both anode and cathode waveforms should be symmetrical with respect to each other. Both cables could be inserted when exposure time was being measured and it was found that the best reading was obtained using an mA trigger because the mA waveform is delayed compared with the kV wave and mA is needed to obtain any X rays. In a similar manner, both cables were connected when readings of the tube filament current were being taken.

When the apparatus is used for initial alignment and calibration of a new installation, both high-tension cables are connected into the high-voltage unit. When alignment is satisfactory, the cathode cable is removed and final adjustments are made. The accuracy of the final alignment is only limited by the design characteristics of the generator-control-tube system.

It has hitherto been thought that a tolerance in final alignment of 10% was all that could be obtained and this has been regarded as acceptable. The design characteristics are such that the present investigation has found that this tolerance can be reduced to 1%, so that previous testing methods were not making full use of the adjustments available.

In use, the Dynalyzer II is easy to connect into any secondary circuit using 75 kVp 3-pin federal-type connectors. On some apparatus from Siemens, special adaptors were found necessary because the retaining ring for the high-tension cable has an internal thread.

The Dynalyzer II test system can readily be transported by one man using a car. The use is specialized in that any one hospital or even one group or area would find it difficult to justify the relatively high cost by the local use that could be found for it. On the other hand, it would seem to be a highly justifiable purchase at the regional level. This apparatus can eliminate guesswork and it takes very little time to produce a complete analysis of performance.

Acknowledgments

It is a pleasure to record the cooperation given by Machlett X Ray Tubes (Great Britain) Ltd. in providing the test apparatus and in always being forthcoming with very useful advice. Dynalyzer is a registered trade-mark of Machlett.

The engineers of all the major apparatus suppliers have assisted in these tests and have enabled us to compare the results obtained on the Dynalyzer II with those of the installation engineers, using their own test equipment. Most of the tests were carried out on new installations in Barnsley District General Hospital (Superintendent Radiographer, A. M. Devine, H.D.C.R.).

Book review

Thermo-Radio-Therapie. Animal Experiments Investigating the Combined Treatment with High Frequency Waves and Röntgen Rays of Solid Ehrlich Ascites Tumours in the Mouse. By Dr. med. habil. Franz Dietzel, pp.124 + 94 references + 96 Appendix with details of results, 1978. (In German) (Urban & Schwarzenburg, Munich) DM48.

ISBN 3-541-08681-5

This book is a published research thesis. It is economically produced in offset-litho with soft covers. It describes experiments carried out over 2–3 years at the University of Giessen on the effect of 461 MHz microwaves and X rays on solid Ehrlich ascites tumours in mice. The experiments were sensibly designed, were well carried out and are well analysed and very clearly described (if I can presume to say so of another language). The literature is adequately listed up to the end of 1976: over 1200 references.

The author used rather short bursts of hyperthermia labelled H1, H2, H3, and H4 respectively because the microwave generator was switched on at a constant 150 W for just one, two, three or four minutes. Temperature versus time curves are given, and are nearly triangular. The times above 37°C were only four, six, eight and ten minutes respectively. The peak temperatures reached momentarily were reported to be about 39.5°, 40.5°, 41.5°, and 42.5° respectively. The author concluded "easily" (unschwer) that hyperthermia alone, given with the aim of healing the tumour, was unrealistic.

X-ray doses of 10, 20, 30 and 40 G were used alone in the control experiments, with acceptable results. Combined treatments were always with 20 Gy, sometimes with simultaneous heating, at other times with an interval between them up to 96 hours. There was little or no effect of the hyperthermia alone on the tumours.

The largest effect was with simultaneous heat and X rays, although intervals shorter than 24 hours were not studied. Dose modifying factors of 1.5 to 2 were found for various parameters of tumour response when heat and radiation were given together, as other authors have found for longer exposures to 42–43°C for one hour. It is surprising that such large DMFs were found for such short exposures. Perhaps microwaves of 461 MHz do have a stronger effect then "waterbath" heating; or were the temperatures actually higher? These DMFs are not higher than those obtained for normal tissues by other authors, whom Dr. Dietzel correctly quotes. This conclusion does not mean that hyperthermia combined with radiotherapy will provide no therapeutic advantages, but it does mean that the advantages have to be sought for by further research and don't just fall off the tree at the first shake.

This book should be on the shelves of researchers into the therapeutic effect of hyperthermia.

J. F. Fowler.

1979, *British Journal of Radiology*, 52, 51–55

Imaging factors for xeroradiography of the extremities

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ABSTRACT

A biological test object has been used to determine optimum imaging factors for xeroradiography of the extremities. Three observers independently demonstrated a clear preference for positive-mode imaging.

When imaging with the Xerox 125 system the operator can select one of three initial plate-charge voltages as well as positive or negative development. In addition, three different development densities can be selected when the negative mode is used. These imaging factors can therefore be varied to give 12 different combinations even before exposure factors, such as kV, are considered.

Good visualization of bone is the main requirement in extremity imaging, although simultaneous visualization of the soft tissues, particularly peri-articular structures, is also important. Use of the positive mode can result in areas of depleted toner around dense structures such as bone and, for this reason, negative mode imaging has been advocated for extremity xeroradiography (Richardson, 1977; Woesner and Sanders, 1972). However, Wolfe (1969) and Gold (1975) appear to use only the positive mode whilst other studies (Luska *et al.*, 1976; Otto *et al.*, 1976) illustrate the use of both positive and negative modes without comment on the respective merits of the two techniques.

The present study attempts to determine optimum imaging factors for xeroradiography of the extremities.

METHOD

An amputated leg was placed on a standard Perspex tunnel and maintained in a constant position. Fifty-six exposures were then made using all combinations of plate charge and development factors with both positive and negative modes. A representative image is shown in Fig. 1A. Radiation exposure factors were constant (Table I) except that with each imaging combination the exposure time was varied to give a range of appearances from under- to over-exposure. Assessment of under- and over-exposure was made as the images were being produced and not every available time-interval between the two extremes was utilized where a single increment of exposure produced no apparent change in the image. The R125 system used employed the standard charge voltages, back bias voltages and number of powder bursts.

Seven areas representing a range of bone and soft tissue appearances were selected and a mask was made with numbered windows through which these areas could be viewed (Fig. 1B). The images with the mask in place were then viewed in a random order by each of the three observers. Each area as seen through the window was scored from 0 to 3 as follows: 0, very poor or absent visualization; 1, structures demonstrated but without much detail; 2, structures reasonably well demonstrated with good detail; 3, structures well shown with fine detail. The random order of viewing the images was different for each observer. This process was then repeated on a separate occasion (with different random orders) so that each observer had eventually viewed and scored all the images twice, each time in a different order.

The scores so obtained were examined to determine the reliability of the image assessment process and to determine the optimum imaging factors for bone areas and soft tissue areas separately, as well as overall.

TABLE I

EXPOSURE FACTORS (3-PHASE GENERATOR)

kV	120	Filtration	2.5 mm Al
mA	200	Time	0.02–0.25 sec
FFD	100 cm	Focal spot	1 mm

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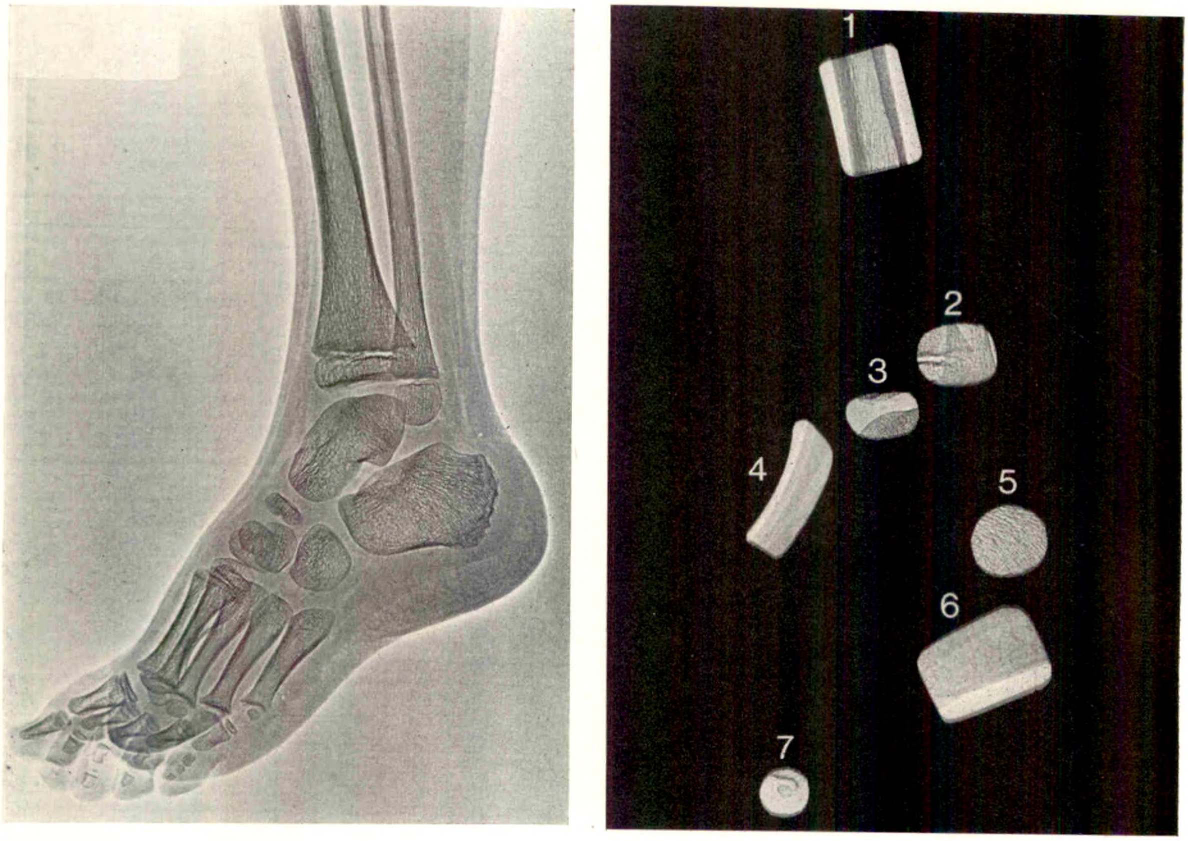

FIG. 1.

(A) An image of the test object (positive mode).

(B) The same image with the mask in position.

ANALYSIS AND RESULTS

The total observed variability in the scores, as measured by their sum of squares about the mean, was split into its component parts as shown in the analysis of variance in Table II. When each sum of squares is divided by the appropriate degrees of freedom, the mean square column is derived. In the absence of any real effect the figures in this column would all be approximately equal to each other, and comparing their size gives an indication of the relative degree of importance of each of the sources of variability. In this instance it is thought unwise to apply the usual significance test that often accompanies such a table, because its underlying assumption of "normal" variability with constant variance cannot be justified when the scores are restricted to only the four values, 0, 1, 2 and 3.

Examination of the table shows that the most important effect is "between images" (*i.e.* consistent differences between one picture and another, after the other relevant effects have been allowed for), followed closely by differences "between observers" and "between areas". The very small figure for "between runs" is a little surprising (the sum of squares taken to more figures is in fact 0.0017), but this indicates only that there was virtually no *consistent* difference between runs. That there was an inconsistent difference (run 1 scoring higher than run 2 for some observers, run 2 higher than run 1 for others) is shown by the mean square for the "interaction between observers and runs", which is the highest of the interactions. Those between "observers and areas", "images and areas" and "observers and images" are the next most important. The other terms, including all the second-order interactions, appear to be negligible.

The main interest in the study lies in the consistent differences between the 56 images, and due to

TABLE II
ANALYSIS OF VARIANCE

Source of variation	Sum of squares	Degrees of freedom	Mean square
Main effects			
Between observers	21.5	2	10.8
Between runs	0.0	1	0.0
Between images	771.9	55	14.0
Between areas	60.6	6	10.1
Interactions			
Observers and runs	9.3	2	4.6
Observers and images	149.9	110	1.4
Observers and areas	36.9	12	3.1
Runs and images	23.5	55	0.4
Runs and areas	2.0	6	0.3
Images and areas	574.6	330	1.7
Second order interactions			
Observers and runs and images	49.0	110	0.4
Observers and runs and areas	4.0	12	0.3
Observers and images and areas	175.3	660	0.3
Runs and images and areas	49.6	330	0.2
Residual	108.7	660	0.2
Total	2036.8	2351	

the balance of the experiment these may be examined in terms of their means knowing that the other effects will cancel out. These means are shown in Table III, where it is evident that *all* means greater than two refer to positive images.

Further analyses of variance (not shown here), taking the positive images and the negative images separately, gave very similar results to the overall analysis except that the "between observers" figure was much greater for the positive images but negligible for the negative images. It remains true that each of them preferred the positives to the negatives, but all regarded the negatives about equally, while varying in their respective enthusiasm for the positives.

A comparison was made between two bone areas combined and two soft tissue areas combined (Fig. 2). It is seen that the positive images do best for the bone areas, while some of the negative images do well for the soft tissue areas. Positive images with a C or D charge do well for both areas.

The relationship between mean score and exposure is shown graphically for the three positive mode techniques in Fig. 3. It can be seen that exposure latitude is greatest with the highest charge (D) and least with the lowest charge (B).

TABLE III
MEAN SCORE PER AREA FOR EACH IMAGING COMBINATION OVER A RANGE OF mAs VALUES

Imaging factors			mAs							
Mode	Density	Charge	4	6	10	16	25	32	40	50
Negative	B	B		1.10	1.81	1.67	1.29	1.12		
		C			1.21	1.17	1.29	1.64	1.33	
		D				0.86	1.31		1.31	0.76
	C	B		1.45	1.55	1.57	1.12	0.45		
		C			1.55	1.79	1.36	1.38	0.60	
		D					1.64	1.83	1.10	
	D	B		1.95	1.64	1.67	1.69	0.31		
		C				1.55	1.38	0.90	1.21	
		D					1.64	1.29	0.90	0.48
Positive		B		1.93	2.33	2.55	2.12	0.55		
		C	1.14	2.26	2.55	2.52	2.48	1.36		
		D	2.19	2.24		2.48	2.31	2.38		

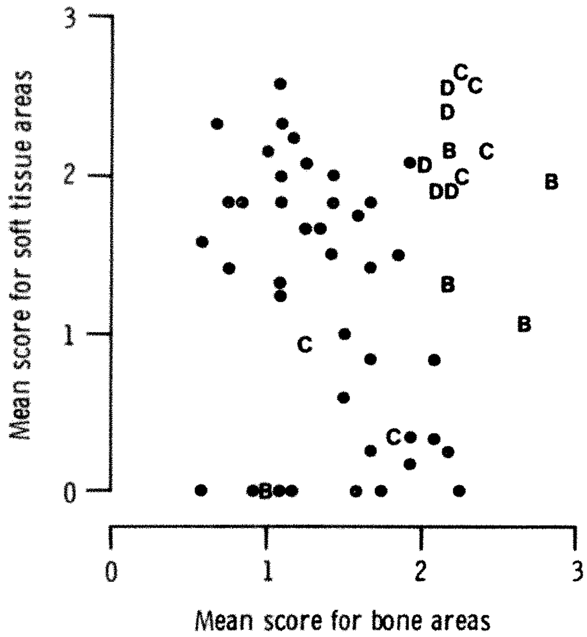

Fig. 2.

The mean scores for two soft tissue and two bone areas compared. (Positive mode images are letters with the letter indicating the charge, negative mode images are dots.)

Discussion

The range of exposures selected appears satisfactory for most imaging combinations since a reduction in mean score on either side of a maximum has been demonstrated. However, for the three negative mode, D density combinations, the maximum score is achieved by the lowest exposure and it is therefore possible that a further exposure reduction would have resulted in a higher score. On re-examination, those images in fact show poor visualization of thicker bony structures due to the high residual charge resulting in poor or absent deposition of powder. Reducing the exposure further would only worsen this problem and an increase in mean score is considered unlikely.

This study indicates that depletion of toner at bone edges when using positive mode imaging does not significantly detract from image quality in extremity xeroradiography and the positive mode is preferred for this application. In the positive mode, a B charge can give exceptional bone visualization but the range of acceptable exposures is small. The increased exposure latitude when using a D charge permits the use of small exposures with relatively little reduction in image quality. Where both soft

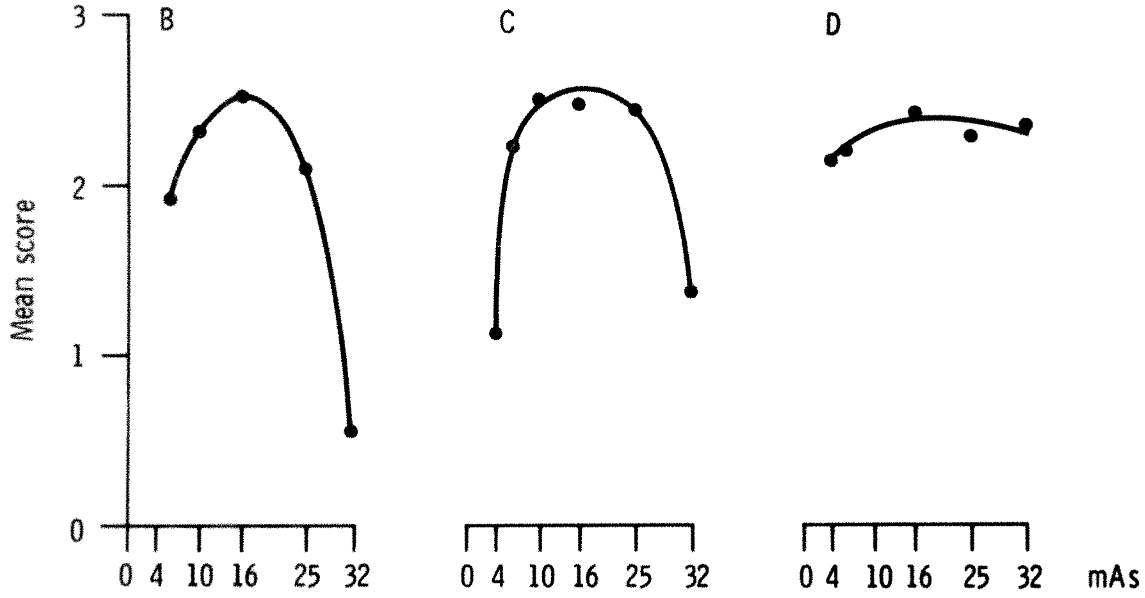

Fig. 3.

The mean score in relation to exposure for each of the three positive mode combinations (B, C and D charge).

tissue and bone visualization is required a C or D charge is preferred.

ACKNOWLEDGMENTS

The authors wish to thank Dr. K. A. Tonge and Dr. P. Renton for their assistance in scoring the images. One of us (J.D.S.) was supported financially by the Department of Health and Social Security.

REFERENCES

GOLD, R. H., 1975. Standard radiography, arteriography, xeroradiography and xero-arteriography in the evaluation of primary bone tumours. *Frontiers of Radiation Therapy and Oncology*, *10*, 82–110.

LUSKA, G., ZEIDLER, H., STENDER, H. S., and SAURE, D., 1976. Die Wertigkeit der Xeroradiographie in der Diagnostik der Chondrocalcinose. *Radiologe*, *16*, 77–82.

OTTO, R. C., POULIADIS, G. P., and KUMPE, D. A., 1976. The evaluation of pathologic alteration of juxtaosseous soft tissue by xeroradiography. *Radiology*, *120*, 297–302.

RICHARDSON, P. J., 1977. Soft tissue xeroradiography. *Radiography*, *43*, 117–125.

WOESNER, M. E., and SANDERS, I., 1972. Xeroradiography: a significant modality in the detection of non-metallic foreign bodies in soft tissues. *American Journal of Roentgenology*, *115*, 636–640.

WOLFE, J. N., 1969. Xeroradiography of the bones, joints and soft tissues. *Radiology*, *93*, 583–587.

1979, *British Journal of Radiology*, *52*, 56–60

Renal consequences of irradiation of the spleen in lymphoma patients

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Abstract

The authors have studied the consequences of irradiation of the upper part of the left kidney during treatment of the spleen. Seventy-four patients with lymphoma were entered in the study. They have all been followed up for between three and five years. Renal function was assessed by physical examination, biological tests, intravenous pyelograms and nephrotomographies, isotope scans with ^{197}Hg neohydrin, dynamic studies with ^{131}I hippuran and ^{99}Tc^{m} DTPA. No significant changes have been noted for blood pressure, biological tests or IVP. Eighteen months after irradiation renal tomograms showed cortical atrophy of the superior pole of the left kidney. ^{197}Hg neohydrin started to show reduced uptake of the isotope in the irradiated region of the left kidney by the eighth month. ^{131}I hippuran and ^{99}Tc^{m} DTPA detected abnormalities respectively five and three months after irradiation. No compensatory hypertrophy nor change in the overall kidney function have been noted.

In Hodgkin's disease, radiotherapy has proved its efficiency in splenic involvement and the lack of secondary renal side effects. On the other hand, morbidity was shown to occur in 5% of cases after splenectomy. From these data, it is proposed to prefer radiotherapy rather than surgery for splenic treatment.

Although the effects of bilateral renal irradiation are well known from the work of Kunkler *et al.* (1952), little is known of the effects of partial or complete irradiation of one kidney. In the course of a clinical trial (Tubiana *et al.*, 1977), comparing the curative value of splenic irradiation versus splenectomy, we started in 1972 to study renal function prospectively in lymphoma patients one of whose kidneys was partially irradiated during splenic radiotherapy. Renal function was assessed using X rays, isotope scans, and clinical and biological tests. The methods of treatment and investigations as well as preliminary results on 16 cases have already been reported (Le Bourgeois *et al.*, 1975).

Materials and Methods

Seventy-four patients were entered in the study of whom 63 were cases of Hodgkin's disease while 12 were cases of non-Hodgkin's lymphoma. The group had a mean age of 30±14 years with a range of four to 67 years. All patients have been followed up for between three and five years. One patient, not in the trial, whose renal function was not assessed prior to radiotherapy has been followed up for 11 years.

Radiotherapy

The spleen was irradiated through anterior and posterior fields using 25 MV photons from a linear accelerator. 4000 rad central dose was delivered in four weeks in four fractions per week. The limits of the splenic fields were identical in all patients including the lower 1–2 cm of the base of the left lung and the left thoracic wall. Medially the field was continuous with the lumbar para-aortic field. The lower border was determined by a spleen scan done in the treatment position. The area of kidney irradiated was measured on the planning check film or the size of the irradiated zone was calculated by proportion from the intravenous pyelogram (IVP). Between 30 and 80% of the kidney was irradiated with a mean of 50%. Two cases with non-Hodgkin's lymphoma of the stomach received 1500 and 4500 rad respectively to the whole of the left kidney.

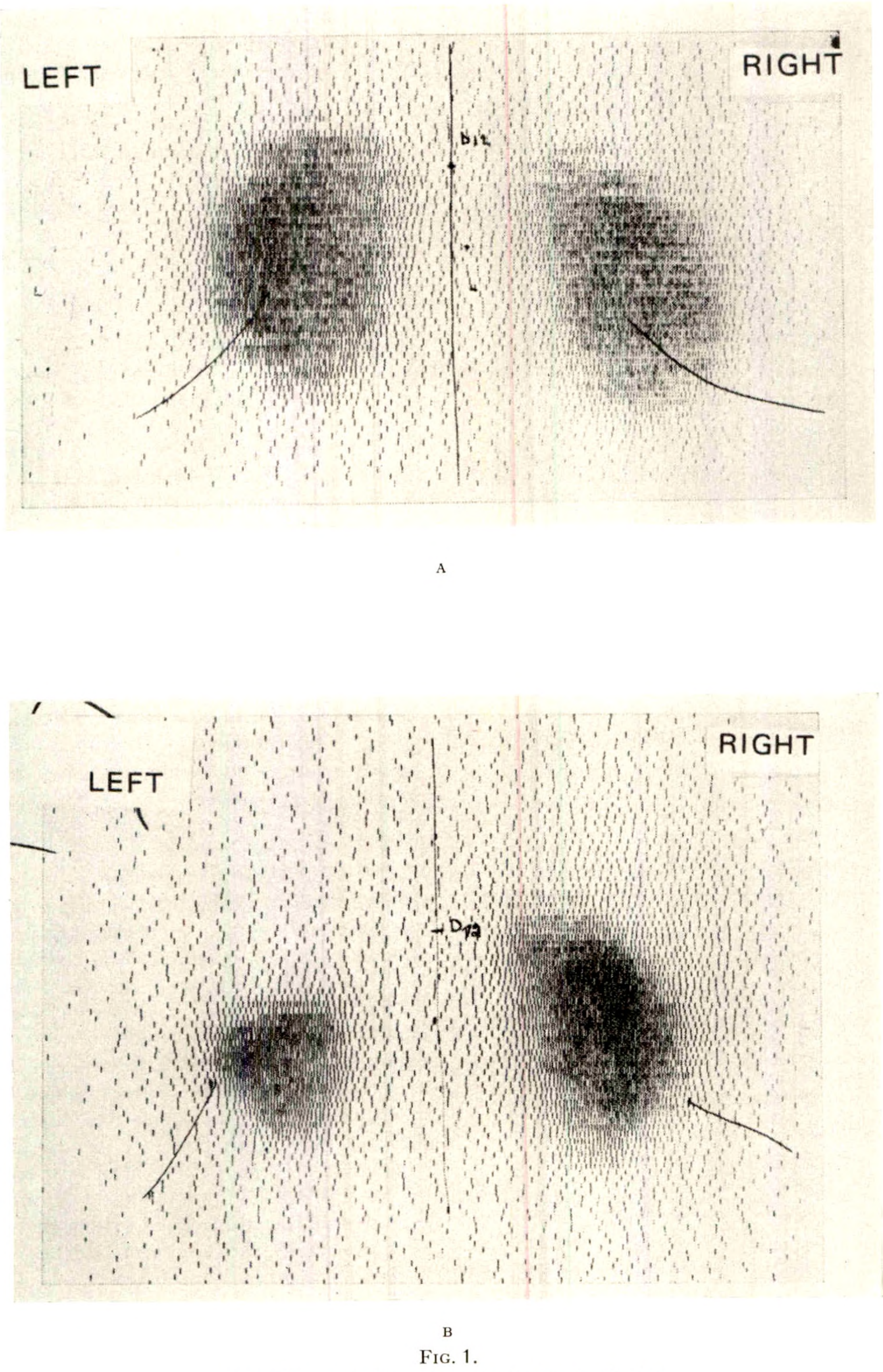
Investigations

Renal function was studied before radiotherapy and after treatment at six weeks, six months, one year and every subsequent year.

The following measurements were made: arterial pressure after lying down for 15 minutes and then on standing; blood urea and creatinine levels, creatinine and urea clearance in three hours, 24 hours urinary protein, and estimation of the number of red and white blood corpuscles in the urine per minute. Measurement of plasma renin levels were obtained in five patients. One patient had bilateral renal vein catheterization with estimation of plasma renin levels from each kidney (Vaughan *et al.*, 1973); an IVP using radio selectan was done at each follow up. Fourteen patients had renal tomography performed during the first minute after injection of the contrast medium.

Two types of isotope studies were performed:

(1) Digital scanning after intravenous injection of ^{197}Hg neohydrin which is filtered by the renal tubules and concentrated in the renal cortex. A posterior scan was performed three hours after



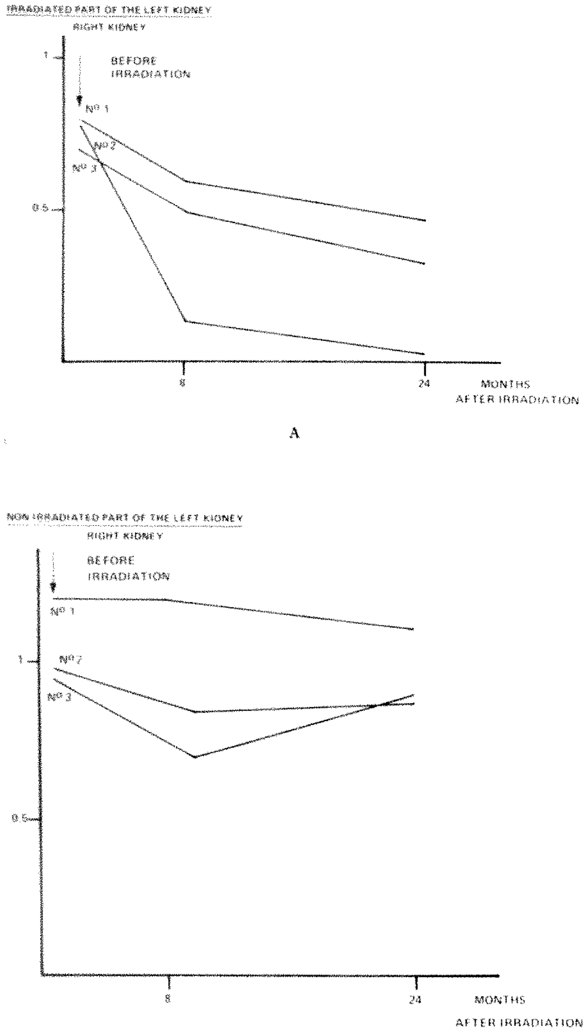
A

B

FIG. 1.

(A) ^{197}Hg neohydrin scintigram before irradiation.

(B) ^{197}Hg neohydrin scintigram eight months after irradiation showing decreased uptake of the upper part of the left kidney.



A

B

Fig. 2.

(A) Time course of the ratio between the mean uptake of ^{197}Hg neohydrin in the irradiated part of the left kidney and the right kidney for three patients (No1, 2 and 3).

(B) Time course of the ratio between the mean uptake of ^{197}Hg neohydrin in the non-irradiated part of the left kidney and the right kidney for three patients (No1, 2 and 3).

intravenous injection of 300 μCi of ^{197}Hg neohydrin. The digital scanner enabled quantitative comparison to be made between uptake in different regions of the kidney. Thus it was possible to calculate the ratio of the uptake in the left kidney to that in the right kidney, as well as to compare the uptake in the upper and lower pole of the same kidney (Le Bourgeois *et al.* 1975).

(2) Dynamic studies of renal plasma flow and of the glomerular filtration rate were carried out with ^{131}I hippuran and ^{99}Tc^{m} DTPA using a scintillation camera on-line with a computer. 300–400 μCi of ^{131}I hippuran or 2 mCi of ^{99}Tc^{m} DTAP were injected 30 minutes after an oral waterload of 1000 ml and the isotope uptake in the two kidneys followed during 30 minutes. Using a computer program we were able to calculate the time course of the activity in each part of the kidney.

Results

The arterial blood pressure did not change in any of the patients. In particular there was no change in blood pressure in a 60-year-old man, three years after he had received 4500 rad to the whole of the left kidney, in spite of the fact that considerable atrophy of this kidney did develop.

Proteinuria of less than 1 g in 24 hours was detected in three cases, and an increase in the number of white blood cells per minute in the urine (between 2000 and 20000) was detected in seven cases. This leucocytosis was accompanied by microscopic haematuria in two cases (4000 and 20000 RBC/min respectively). These changes were detected by the eighth month following radiotherapy and subsequently disappeared. In all other cases there was no proteinuria and the RBC and WBC loss was always below 500 cells of each type per minute.

The creatinine clearance was normal in all cases. Plasma renin levels stayed within normal limits in all the five cases in which they were measured. There was no increase in the plasma renin levels in the right and left kidney of the patient who had received 4500 rad to the entire kidney at 24 months post treatment. As the hippuran renogram showed that plasma flow in the left kidney was only 20% of that in the right kidney, renin secretion by the left kidney must have been one fifth of that of the right kidney.

No morphological changes were detected in the standard IVP of any patient following partial renal irradiation. The patient who had received 4500 rad to the entire left kidney had one minute delay in excretion of the contrast, first detected two years after irradiation. However, there was no modification in the appearance of renal calyces.

The size of the irradiated kidneys diminished for 30 months after irradiation. The degree of reduction in size ranged from 1 to 4 cm depending upon whether the irradiation was partial or total. During the same period the size of the right kidney did not change. Sometimes the lower pole of the irradiated kidney appeared to rise. No compensatory hypertrophy of the right kidney, or the lower pole of the left kidney, was observed.

Eighteen months after irradiation, renal tomograms showed cortical atrophy of the superior pole of the left kidney with a reduction in the cortical index, contraction and stenosis of the superior calyceal channels and flattening of the renal papillae in the irradiated region.

The ^{197}Hg neohydrin scintigrams started to show reduced uptake of the isotope in the irradiated region of the left kidney by the eighth month (Fig. 1). Computer data showed that uptake was reduced by about 70% in the irradiated region and 20–30% in the non-irradiated region. The uptakes decreased slowly until the twentieth month, after which they stabilized but showed no signs of improvement (Fig. 2).

The ^{131}I hippuran renogram showed a mean delay of two minutes in the appearance of the peak at the level of the irradiated portion of the kidney in 11 cases studied, with a 30–50% reduction in the height of the peak when compared to the peak of the normal kidney. The height of the peak in the unirradiated portion of the left kidney was intermediate between the peak from the right kidney and that from the irradiated portion of the left kidney. These changes were first detected five months after irradiation. On the other hand, from three months after irradiation isotopic uptake in the irradiated portion of the left kidney was reduced on the DTPA scans, in spite of the fact that the ^{131}I hippuran scan was normal at that time.

DISCUSSION

The absence of hypertension in these patients could be explained by destruction of the sites of renin production (Ljungquist *et al.*, 1971), or by a protective mechanism exerted by the contralateral kidney (Vaughan *et al.*, 1973). The normal renin levels observed in our cases exclude frank elevation of renin secretion after radiotherapy and rather suggest a reduction in renin production.

The slight changes observed in the biochemical parameters are probably due to an interstitial nephropathy and have already been reported in the literature after bilateral renal irradiation (Luxton, 1953). The absence of an elevated creatinine level is not surprising since more than 50% of the functioning nephrons must be damaged before any elevation of creatinine becomes apparent (Davey *et al.*, 1952).

Our results confirm the great sensitivity of isotope tests in detecting post-radiotherapy damage (Quinn *et al.*, 1962). The reduced uptakes observed in ^{197}Hg neohydrin and ^{99}Tc^{m} DTPA scans appear before any lesions are detectable on IVP or renal tomograms. In fact, the IVP in the case of a unilateral nephropathy often gives excellent opacification of the renal calyces due to increased concentration of the excreted iodide, present in a reduced volume of urine (Bitker *et al.*, 1969). Eight months after radiotherapy glomerular and tubular damage is present, but can only be detected isotopically. This damage leads to the later changes already described elsewhere (Madrago *et al.*, 1970; Mostofi *et al.*, 1964; Rich *et al.*, 1961; Russell, 1953). The reduction in isotope uptake appears after 1500 rad delivered in 18 days to the whole kidney. The kidney is therefore more radiosensitive than has been thought (Luxton, 1953). The changes detected on renal tomography seem to be due to fibrosis and, when they are established, do not progress.

We did not detect any evidence of compensatory hypertrophy of the other kidney or of the remaining portion of the irradiated kidney. In fact this hypertrophy observed in animals when the two inferior poles of the kidneys have been irradiated (Asscher, 1964) is not usually observed in human cases of unilateral nephropathy (Raynaud, 1973). The absence of compensatory hypertrophy suggests that there is no alteration in the overall kidney function.

CONCLUSIONS

Partial irradiation of a kidney leads to local sequelae which are clinically and biologically well tolerated for up to five years. Isotopic methods are especially valuable for the early detection of these lesions which do not progress after the second year.

No significant difference in relapse rate could be shown between patients treated with splenectomy or with splenic irradiation.

Thus splenic radiotherapy has proved its efficiency and its safety since no clinical renal sequelae could be detected in the patients so far treated.

On the other hand, morbidity was shown to occur in 5% of cases after splenectomy. From these data, it is proposed to prefer radiotherapy rather than surgery for splenic treatment in Hodgkin's disease.

REFERENCES

ASSCHER, A. W., 1964. The delayed effects of renal irradiation. *Clinical Radiology*, *15*, 320–325.

BITKER, M., CHATELAIN, C., GUEDON, J., and KUSS, R., 1969. L'urographie dans certaines néphropathies unilatérales. *Journal of Urology and Nephrology*, *75*, 76–89.

DAVEY, P. W., HAMILTON, J. D., and STEELE, H. D., 1952. Radiation injury of kidney. *Canadian Medical Association Journal*, *67*, 648.

KUNKLER, P. B., FARR, R. F., and LUXTON, R. W., 1952. The limit of renal tolerance to X rays. An investigation into renal damage occurring following the treatment of tumours of the testis by abdominal baths. *British Journal of Radiology*, *25*, 190–201.

Le Bourgeois, J. P., Godefroy, D., Di Paola, M., Parmentier, C., and Tubiana, M., 1975. A propos des néphrites post-radiothérapiques. Etude du rententissement rénal de l'irradiation de la rate dans les hématosarcomes. *Journal of Radiology and Electrology*, *56*, 826–829.

Ljungquist, A., Unge, G., Lagergren, C., and Notter, G., 1971. The intrarenal vascular alterations in radiation nephritis and their relationship to the development of hypertension. *Acta pathologica et microbiologica Scandinavia. Kjøbenhaven*, *79*, 629–638.

Luxton, R. W., 1953. Radiation nephritis. *Quarterly Journal of Medicine*, *22*, 215.

Madrago, H., Juzuki, Y., and Churg, J., 1970. Radiation nephritis chronic changes after high doses of radiation. *American Journal of Pathology*, *61*, 31–44.

Mostofi, F. K., Pani, K. C., and Ericsson, J., 1964. Effects of irradiation on canine kidney. *American Journal of Pathology*, *44*, 707.

Quinn, J. L., Meschan, I., Blake, D. D., and Witcovski, R. L., 1962. The usefulness of the radioisotopic renogram in radiation therapy. *Radiology*, *78*, 266–268.

Raynaud, C., 1973. In *La fixation rénale du mercure radioactif* (Masson et Cie-Editeurs-Paris).

Rich, J. G., Glagov, S., Larsen, K., and Spargo, B., 1961. Histochemical studies of rat kidney after abdominal X-irradiation. *Archives of Pathology*, *72*, 388–409.

Russel, L. H., 1953. Renal sclerosis post-radiation nephritis following irradiation of the upper abdomen. *Edinburgh Medical Journal*, *60*, 474.

Tubiana, M., Mathe, G., Hayat, M., Le Bourgeois, J. P., Henry Amar, M., and Laugier, A., 1977. Le traitement des stades cliniques I et II de la Maladie de Hodgkin. *Nouvelle Revue Française D'Hématologie*, *18*, 463–472.

Vaughan, E. D., Buhler, F. R., Lanagh, J. H., Sealey, J. E., Baer, L., and Bard, R. H., 1973. Renovascular hypertension: renin measurements to indicate hypersecretion and contralateral suppression estimate renal plasma flow and score for surgical curability. *American Journal of Medicine*, *55*, 402–414.

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The recovery of iron uptake in erythropoietic bone marrow following large field radiotherapy

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ABSTRACT

Large X-ray fields, such as those used to irradiate major lymph-node areas in the treatment of lymphomas, often irradiate large areas of haemopoietic bone marrow. The absorbed doses received by the marrow are close to the tolerance level.

Quantitative scanning of the bone marrow, using ^{52}Fe and a digital whole-body scanner, has been carried out in a series of 22 patients treated by radiotherapy up to nine years previously in order to assess the extent and recovery of their erythropoietic marrow.

The results showed large variations from patient to patient; in some patients the iron uptake in the marrow returned to near normal levels in two to three years, while in others the uptake remained suppressed after seven to eight years. The tolerance dose for the bone marrow appeared to be about 1100 ret. There was some evidence of a more rapid recovery of erythropoietic function in males than females, but no evidence to show that age of patient, type of disease or whether chemotherapy had been used influenced the results. Patients who showed a decreased iron uptake in an irradiated region of marrow generally showed a compensating increased uptake in unirradiated regions, which in some cases was associated with anaemia.

Large X-ray fields are now commonly used in the radiotherapy of patients with Hodgkin's disease and other lymphomas. Such large fields, which are designed to irradiate the major lymph node areas to high doses (over 3000 rad in about four weeks), also irradiate major areas of haemopoietic tissue in adult patients. The absorbed doses received by the bone marrow are very close to the tolerance dose reported by Sykes *et al.* (1964). The work of these authors was based upon sternal aspirations in localized breast cancer in patients who had received doses up to 6000 rad in six weeks. Above 3000 rad in three weeks (1140 ret), 54 of 56 patients showed little or no marrow regeneration in the sternum. Vogel *et al.* (1968) also have demonstrated decreased bone-marrow reserve in patients who have undergone extensive radiotherapy. The depressive effect of irradiation on the marrow has been demonstrated, by qualitative scanning of radiopharmaceuticals that are taken up in the marrow, by a number of authors who have noted the time lapse before the marrow uptake re-appears on a scan. Bell *et al.* (1969) and Rubin *et al.* (1973) used ^{99}Tc^{m}-S colloid and concluded that the reticulo-endothelial activity of the marrow remained depressed for one to two years following a fractionated course of radiotherapy. DeGowin *et al.* (1974) used ^{59}Fed to visualize the marrow and came to similar conclusions on the time of depression of erythropoietic activity.

The purpose of the present study was to assess, by quantitative scanning of the marrow using ^{52}Fe, the extent and percentage recovery of the erythropoietic marrow in patients at various periods after irradiation and to measure the effect on the marrow uptake in the unirradiated areas. The importance of assessing the state of the irradiated marrow is also of relevance when chemotherapy is subsequently considered as this may be an important factor in determining the tolerance of the patient (Curran and Johnson, 1970; Hoogstratten *et al.*, 1973).

METHOD OF STUDY

Two groups of patients were studied: (a) a control group of 17 patients with malignant disease but with normal bone-marrow biopsies and blood counts, who had had neither radiotherapy nor chemotherapy, and (b) a "treatment" group of 22 patients who had had previous large field irradiation of 3000–4000 rad in about three to four weeks (1030–1300 ret) with either ^{60}Co γ rays or 6 MeV X rays. The majority of these patients had a diagnosis of Hodgkin's disease or other lymphoma and the radiotherapy was normally either with "mantle" fields which included cervical, supraclavicular, axillary and mediastinal lymph nodes or with "inverted Y" fields which included para-aortic, pelvic and inguinal nodes. Some patients had both mantle and inverted Y fields and with some only one side of the inguinal node area was irradiated ("dog-leg" field). A summary of the diagnosis and radiotherapy treatment for the treatment group is given in Table I.

All patients were given an intravenous injection of 70 μCi ^{52}Fe (from the MRC Cyclotron Unit,

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TABLE I

Sex, age	Diagnosis	Radiotherapy			Chemotherapy (yes or no)	^{52}Fe uptake (% normal)		Haemoglobin at time of scan (g/l)
		Area*	NSD (ret)	Time elapsed (years)		Treated area	Untreated area	
F, 26	H.D.	1	1595†	0	Y	0–10	150	90
M, 26	H.D.	Mantle	1155	0	N	0–10	170	118
F, 45	H.D.	Chest	1211†	6	Y	40–60	100	89
F, 32	H.D.	Mantle	1206	8	N	80–100	100	145
M, 22	H.D.	Mantle Inv. Y	1368† 1180†	3 3	Y	80–100 80–100	100	142
F, 65	H.D.	Inv. Y	1128	1	Y	0–20	200	88
F, 60	Lymphoma	Inv. Y	1097	6	N	10–20	150	‡
M, 15	H.D.	Mantle	1032	3	N	80–100	100	91
M, 20	H.D.	Mantle	1313	2½	Y	60–80	100	92
F, 47	H.D. stomach	2	1097†	5	Y	50–70	100	95
F, 52	Ca ovary	Pelvis	1113†	¼	N	10–20	100	120
M, 41	Gut lymphoma	Inv. Y	1217	1	N	10–20	140	138
F, 40	Lymphoma	Inv. Y	1176	1¼	Y	30–40	140	125
F, 30	H.D.	Mantle	1232	6	N	10–20	150	133
M, 28	H.D.	Mantle Inv. Y	1251 1228	5¾ 6½	N	80–100 45–55	100	138
M, 33	Seminoma	Dog-leg Mantle	1209 1055	4½ 4½	N	40–60 40–60	120	150
M, 42	Teratoma	Dog-leg	1333	2½	N	0–20	200	149
F, 22	H.D.	Mantle	1196	¾	N	10–20	130	135
M, 69	Seminoma	Dog-leg	1053	6½	N	70–80	120	144
M, 26	H.D.	3	1088	2	N	40–60	100	153
M, 58	Lymphoma	Inv. Y	1128	4	N	20–30	150	138
F, 30	H.D.	Mantle Inv. Y	1203 1178	9 8½	N	70–80 60–70	100	143

*Mantle = mediastinal, cervical, supraclavicular + axillary nodes
Inv. Y = para-aortic, inguinal + pelvic nodes
Dog-leg = para-aortic + one side of inguinal + pelvic nodes
1 = lumbo-sacral spine + para-aortic nodes
2 = stomach + para-aortic nodes
3 = mantle + para-aortic nodes
†Estimate from incomplete radiotherapy data.
‡Not available.
H.D. = Hodgkin's disease.

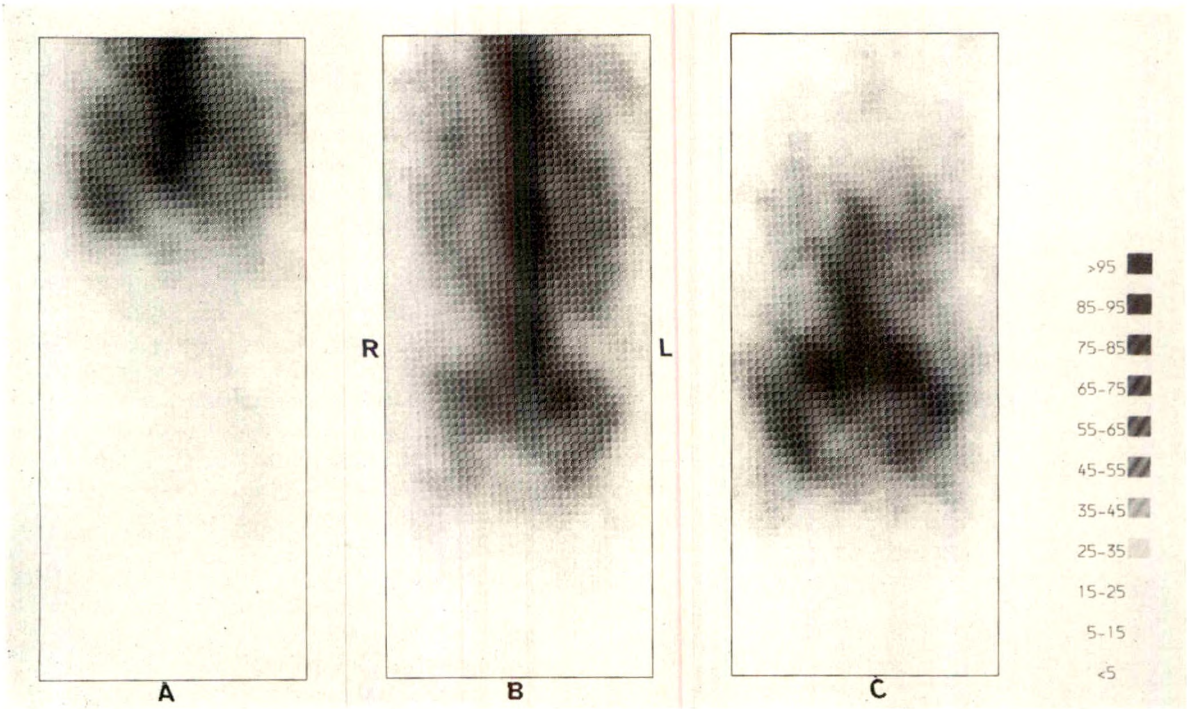

FIG. 1.

Microfilm isocount displays of digital scans 20 hours after intravenous administration of ^{52}Fe. (A) Scan of patient treated with "inverted Y" field one year previously. (B) Normal pattern showing uptake in spine, pelvis and rib cage. (C) Scan of patient treated with "mantle" field six years previously.

Hammersmith Hospital) and were scanned approximately 20 hours later. The resulting absorbed doses to different organs from this activity are given in a previous paper (Lillicrap *et al.*, 1976). The scanner, which is a dual-headed whole-body scanner situated in a low background area, has also been described previously (Cottrall *et al.*, 1973). The digital output from the scanner is fed into a CDC 7600 computer which produces a matrix of counts (the summed output from the two detectors at 2 cm intervals) over the patient, corrected for background. A microfilm isocount display of the numerical data is also produced. Three such displays for different patients are shown in Fig. 1.

The numerical data were examined as follows:

(1) A check was made that the total counts on the scan per μCi at the time of scanning was constant within $\pm 10\%$ for all patients. This indicated that little activity had been excreted by the patient in the period before the scan. A weighed aliquot of the injected dose counted at the same time as the scan served as a standard to allow for corrections for physical decay and instrumental drift.

(2) Several small (approximately 5 cm square) areas were picked out from the scan matrix. These corresponded anatomically to upper, middle and lower spine, sacrum and right and left pelvis. The average count in each of these areas was expressed as a percentage of the total counts in the scan. For the group of patients with a normal bone marrow picture the mean value for the group and the range in each area was found. For the patients who had received radiotherapy the count values for each area were then expressed as percentages of normal.

(3) The isocount displays were examined for any obvious changes in marrow distribution such as extension of the uptake to the long bones or to the skull.

RESULTS AND DISCUSSION

In several patients it was found that uptake of ^{52}Fe in areas treated by radiotherapy was very much reduced even several years after the completion of treatment. Figure 1 (A and C) shows the scans of two patients, one treated six years previously with a "mantle" and the other treated one year previously with an "inverted Y" field. The results for all the patients studied are shown in Fig. 2. Since some

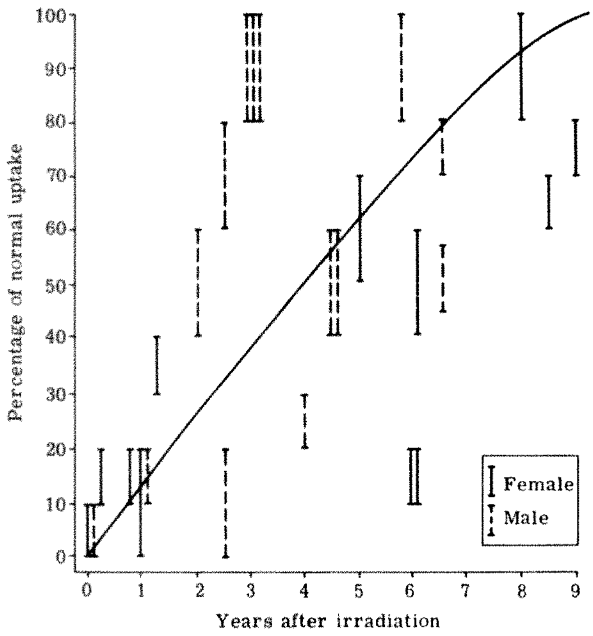

Fig. 2.

Graph of iron uptake (expressed as percentage of normal uptake) in irradiated areas as a function of time after irradiation for 22 patients (26 sites).

patients had more than one area treated (*e.g.* both mantle and inverted Y fields), this graph gives the extent of marrow recovery in irradiated areas. The limits on the points are the estimated errors due to statistical fluctuations, background levels and variation from patient to patient. It can be seen that while for some patients the uptake in the marrow returns to near normal levels in two to three years after irradiation, in other patients the uptake remains suppressed up to seven years later. Fifteen of the 19 areas scanned two years or more after radiotherapy showed at least 40% of the normal uptake in the marrow while only three of the 19 irradiated areas showed no appreciable uptake at all.

However, only eight of the 19 treated areas in this time period showed an uptake in excess of 70% of the normal value which for the present evaluation may be taken as an effective full return to normal values for erythropoietic function. These results are similar to those of Rubin *et al.* (1973) who, in a series of 27 patients, reported, from qualitative scanning of ^{99}Tc^{m} sulphur colloid, that some reticulo-endothelial activity of the marrow had returned after a two year period in about 85% of the patients following absorbed doses of about 4000 rad.

In order to see whether there is any correlation between the marrow recovery rate and any treatment parameter or patient characteristic, various details of the patients and their treatments were examined and are tabulated in Table I. The Ellis (1968; 1971) nominal standard doses (NSD) are used as the parameters to compare treatments which sometimes include rest periods. From the work of Sykes *et al.* (1964) it would appear that 1100 ret to the marrow was the tolerance dose for their patients beyond which no marrow regeneration was observed. In the present series of patients, as the fastest return to normal marrow uptake is observed in about two years, patients who were irradiated more than two years previously have been examined to distinguish between those with a normal marrow uptake and those with a retarded marrow recovery or permanently damaged marrow. In this time period there are ten patients (13 areas) who had received more than 1100 ret, and six patients (six areas) who had received less than 1100 ret. Six of the 13 areas which received more than 1100 ret showed at least 70% of the normal marrow uptake and two of the six areas which received less than 1100 ret showed this uptake. It is seen therefore that there is no sharp break at 1100 ret in the ability of the marrow to recover, and these results are broadly in agreement with those of Sykes *et al.* (1964) that the tolerance dose is about 1100 ret but that individual variations occur among patients. Within the narrow range of NSD observed (about 300 ret) centred around 1150 ret the ability of the marrow to recover is variable. The observations of Sykes *et al.* (1964) covered a much wider range of NSD from 700 to 1700 ret with only a few patients near the tolerance level.

As all the patients in this series have had marrow irradiation close to the tolerance dose the data have been examined to observe whether any other factor appears to influence the ability of the erythropoietic marrow to recover. Seven of the patients had a course of chemotherapy either prior to or immediately following their course of radiotherapy. They all received similar NSD's to the non-chemotherapy patients with a similar proportion showing recovery of marrow uptake. However, the data in this area are sparse and only the general conclusion can be drawn that the difference between the two sets of patients is not great. Curran and Johnson (1970) have examined tolerance to chemotherapy in a series of patients developing relapse of disease after primary treatment with radiotherapy. They report that chemotherapy tolerance improves with time after extensive radiotherapy. They conclude that the relative intolerance to chemotherapy extends well beyond six months after irradiation and that the return of peripheral blood counts to normal does not necessarily predict a normal bone marrow reserve. Thus, if erythopoietic bone-marrow scanning proves to be a more reliable indicator of bone marrow reserve, then such a scan may be of value in assessing potential tolerance to chemotherapy in those patients who have had a relapse of disease after previous radiotherapy.

Androgens, which have been used to encourage the recovery of marrow in patients with aplastic anaemia (Sanchez-Medal *et al.*, 1969), may also influence the ability of the marrow to recover after radiotherapy in males. In Fig. 2, a distinction is made between the results for male and female patients, and a crude mean recovery curve is also shown. Of the eight points which lie considerably below this curve five refer to females, while six of the seven points which lie considerably above refer to males. Thus, there would appear with these few patients to be some suggestion of a more rapid recovery of erythropoietic function in males.

The effect of age and disease type has also been considered. No correlation was observed with either parameter except that the three patients showing the most rapid return to normal uptake values were three young males with Hodgkin's disease aged 15, 20 and 26.

In the patients who showed a decreased marrow uptake in the irradiated region there was generally a compensating increased uptake of ^{52}Fe in the areas of unirradiated erythropoietic marrow. This effect is shown in the penultimate column of Table I where patients who had either thoracic or abdominal irradiation are tabulated with the typical uptakes in both the irradiated and unirradiated areas given as percentages of normal. In none of these patients was there any extension of the uptake of ^{52}Fe beyond the normal limits in the adult. Thus it would appear that where part of the normal distribution of erythropoietic narrow is damaged by irradiation, there is an increase in the iron uptake in the unirradiated erythropoietic marrow, and not an extension of activity to include the long bones of the skeleton. The final column of Table I shows relevant haemoglobin values. It can be seen that increased uptake of ^{52}Fe in unirradiated areas, which may reflect increased erythropoietin activity in the patient, does not necessarily result from anaemia.

In one case extension of the marrow uptake to the femora and the knees was observed. However, as this was a patient of 15 years this may well have been consistent with his age. In none of the cases studied was there any evidence of extramedullary haemopoiesis.

CONCLUSIONS

The present clinical study of erythropoietic marrow using ^{52}Fe has led to the following conclusions:

(1) The normal tumouricidal dose of about 1100 ret in patients receiving large field radiotherapy is close to the tolerance dose for erythropoietic marrow recovery. The tolerance level varies from patient to patient with males appearing to have a slightly higher tolerance level than females.

(2) One year appears to be the minimum time before the marrow uptake of iron begins to recover.

(3) When one section of the normal erythropoietic marrow is irradiated resulting in a suppression of the iron uptake, there is a compensating increase in iron uptake in the remaining unirradiated erythropoietic marrow. No extension of uptake outside the normal adult distribution of erythropoietic marrow was observed.

(4) When patients return for chemotherapy with relapse of disease following radiotherapy, a quantitative erythropoietic marrow scan may prove a useful guide to chemotherapy tolerance.

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REFERENCES

BELL, E. G., MCAFEE, J. G., and CONSTABLE, W. C., 1969. Local radiation damage to bone and marrow demonstrated by radioisotopic imaging. *Radiology*. *92*, 1083–1088.

DEGOWIN, R. L., CHAUDHURI, T. K., CHRISITE, J. H., CALLIS, M. N., and MUELLER, A. L., 1974. Marrow scanning in evaluation of hemopoiesis after radiotherapy. *Archives of Internal Medicine*, *134*, 297–303.

COTTRALL, M. F., HODT, H. J., KENT, R. W., and TROTT, N. G., 1973. Investigations using a whole-body scanning system with digital control and read-out. In *Radioaktive Isotope in Klinik und Forschung*. Ed. K. Fellinger and R. Hofer, *10*, pp. 45–47 (Urban & Schwarzenberg, Munich).

CURREN, R. E., and JOHNSON, R. E., 1970. Tolerance to chemotherapy after prior irradiation for Hodgkin's disease. *Annals of Internal Medicine*, *72*, 505–509.

ELLIS, F., 1968. The relationship of biological effect to dose-time-fractionation factors in radiation therapy. In *Current Topics in Radiation Research*. Ed. M. Ebert and A. Howard, *4*, 359–397 (North-Holland Publishing Company, Amsterdam).

1971. Nominal standard dose and the ret. *British Journal of Radiology*, *44*, 101–108.

HOOGSTRATTEN, B., HOLLAND, J. F., KRAMER, S., and GLIDEWELL, O. J., 1973. Combination chemotherapy—radiotherapy for stage III Hodgkin's disease. An acute leukaemia group B study. *Archives of Internal Medicine*, *131*, 424–428.

LILLICRAP, S. C., STEERE, HEATHER, and CLINK, H. M., 1976. Distribution and dosimetry of ^{52}Fe and ^{59}Fe in bone marrow and other organs. In *Radioaktive Isotope in Klinik und Forschung*. Ed. R. Hofer, *12*, 79–90. (Egermann).

RUBIN, P., LANDMAN, S., MAYER, E., KELLER, B., and CICCIO, S., 1973. Bone marrow regeneration and extension after extended field irradiation in Hodgkin's disease. *Cancer*, *32*, 699–711.

SANCHEZ-MEDAL, L., GOMEZ-LEAL, A., DUARTE, L., and RICO, MARIA G., 1969. Anabolic androgenic steroids in the treatment of acquired aplastic anaemia. *Blood*, *34*, 283–300.

SYKES, MARGUERITE P., CHU, FLORENCE C. H., SAVEL, H., BONADONNA, G., and MATHIS, HAZEL, 1964. The effects of varying dosages of irradiation upon sternal-marrow regeneration. *Radiology*, *83*, 1084–1088.

VOGEL, J. M., KIMBALL, H. R., FOLEY, T., WOLFF, S. M., and PERRY, S., 1968. Effect of extensive radiotherapy on the marrow granulocyte reserves of patients with Hodgkin's disease. *Cancer*, *21*, 798–804.

1979, *British Journal of Radiology*, 52, 67–74

A plethysmographic method for measuring function in locally irradiated mouse lung

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ABSTRACT

A plethysmograph has been developed to measure pulmonary function in mice after single doses of X rays to both lungs. The apparatus consists of a whole-body airtight chamber fitted with a Lavalier microphone. The microphone acts as a sensitive electrical capacitance manometer converting pressure changes in the chamber into an electrical signal which is electronically processed and recorded on a pen recorder. Two parameters of lung function were simultaneously monitored, breathing rate and amplitude.

Lung function has been tested in male CBA mice aged two to six months and in animals which have received graded X-ray doses to both lungs. No diurnal rhythm or age-related increase has been observed up to six months in control mice. The two lung-function parameters exhibited a dose-dependent response in irradiated lungs tested 16 weeks after irradiation; the response was reproducible in successive experiments. Respiration rate was increased above a threshold dose of 11 Gy (1100 rad), while amplitude decreased, also with a threshold at 11 Gy. These changes were observed before histological evidence of fibrosis became apparent and before pulmonary insufficiency led to deaths in the higher dose groups.

The measurement of lung function by plethysmography is an alternative to lethality for assessing radiation damage in the lungs of small animals. The technique is non-destructive, responding to lower doses than LD_{50}, and allows quantitative assessment of sequential changes in the lungs in each mouse over long post-irradiation times.

New quantitative endpoints for the assessment of normal tissue injury after irradiation are being developed by an increasing number of investigators (Chauser *et al.*, 1976; Glatstein *et al.*, 1975; Hayashi and Suit, 1971; Hirst *et al.*, 1977; Hopewell, 1975; Stewart, 1977; Van der Kogel *et al.*, 1977; Vatistas and Hornsey, 1966; White and Hornsey, 1977; Withers, 1967; Withers and Elkind, 1969). Because radiation damage to normal tissues is the dose-limiting factor in radiotherapy it is important that endpoints should be established which enable injury, particularly late injury, to be quantitated. Many of the techniques presently available are invasive or involve sacrifice of the animal. Functional assays which permit sequential assessment of injury in the same groups of animals over a period of time are available for only a few organs in small laboratory animals.

The present study reports a new non-invasive technique of measuring changes in pulmonary function after irradiation of both lungs of mice.

MATERIALS AND METHODS

Experimental animals and radiation procedures

Lung function was tested in mice in which both lungs were irradiated and in sham-irradiated controls. Male CBA/Ht mice, 10–12 weeks old, were given single doses of X rays ranging from 8 to 20 Gy. Radiation was delivered with a 250 kV X-ray unit, operated at 240 kV with an HVT of 1.3 mm Cu at a target skin distance of 20 cm. The dose rate was 3.65 Gy per min. Four mice were irradiated simultaneously on a specially constructed jig. The total dose was delivered within four to ten minutes in four equal increments with the jig rotated 90 deg after each increment to allow for a constant 10% dose-difference between the four irradiation positions. Both lungs were irradiated through two anterior 20 × 15 mm apertures in a 3.0 mm thick lead shield which protected the remainder of the body. Structures in the thoracic mid-line were also protected by a 1.0 mm wide strip in the lead shield separating the two lung fields. Perspex pillars fixed to the base of the jig kept the mouse in a supine non-rotated position and held the rib cage in position with respect to the radiation fields. This positioning was checked in some animals by radiographs which showed that less than 5% of the total volume of lung was protected by the mid-line shield. Dose distribution in the lung was checked using thermoluminescent dosimeters in dead mice.

The mice were anaesthetized before irradiation with sodium pentobarbital (60 mg/kg) given intraperitoneally. Megimide (15 mg) was given to each mouse after irradiation to speed recovery from the anaesthetic.

Pulmonary function was measured at monthly intervals up to 26 weeks in the control group and at 16 weeks in the irradiated groups. A specially constructed total body plethysmograph, described below, was used to assess pulmonary function.

Equipment and electronics

The changes in thoracic gas volume during respiration can be measured by using a whole-body plethysmograph and a sensitive electrical capacitance manometer. The design of the apparatus used in the present experiments was based on the larger apparatus commonly used for measuring lung function in human subjects.

The plethysmograph was a clear Perspex airtight cylinder with a volume of 125 cm^3, both ends of which could be opened (Fig. 1). One end was fitted with a wire mesh screen and, immediately outside it, a hinged door. This allowed the cylinder to be opened without releasing the mouse. The mouse was placed in the chamber at the opposite end which was then closed by a removable door. The chamber was airtight when both ends were closed.

The pressure transducer was a modified Lavalier microphone (Mytex TMX 1250) which acted as the electrical capacitance manometer. The microphone was housed in the removable door of the chamber and responded to pressure changes in the whole chamber. One side of the microphone diaphragm was exposed and in direct contact with the gas in the chamber. The other side of the diaphragm was maintained in pressure equilibrium with the atmosphere through a narrow tube which had a high acoustic impedance except at very low frequencies. The diaphragm and a fixed backplate formed a capacitor. Capacitance changes were translated into voltage changes by having a permanent electrical charge impressed on the diaphragm (electret element; Fraim and Murphy, 1970). These voltage changes were amplified by a high impedance buffer amplifier close to the capsule. The overall frequency response was determined by the input impedance of the amplifier ($> 10^{10}\,\Omega$) and by the dimensions of the tube for pressure equalization. The low frequency cut-off (-3 dB) of the modified microphone unit was 1.2 Hz.

Initial experiments with the transducer indicated that further filtering was required to remove interfering signals that were not associated with respiration. It was also determined that the breathing rate of the mice was in the range 4–10 Hz. This is a higher value than reported in the literature but it has been checked by further experiments. The signal was therefore electrically filtered to exclude frequency components below about 3.3 Hz (arising due to movement, temperature changes, etc.) and above about 11 Hz (due to sounds of scratching, sniffing, etc.). From measurements on unfiltered signals it was found that a rate of 24 dB per octave would be necessary for the high-pass filter while a 12 dB per octave low-pass filter would be sufficient. To obtain the optimum characteristics the final response was trimmed to provide minimum overshoot consistent with the required cut-off slopes as this was considered more important than the precise cut-off frequency. The resulting filtered signal could be monitored on an oscilloscope or a chart recorder at this stage. The action of the filters on the signal from the transducer is shown in Fig. 2.

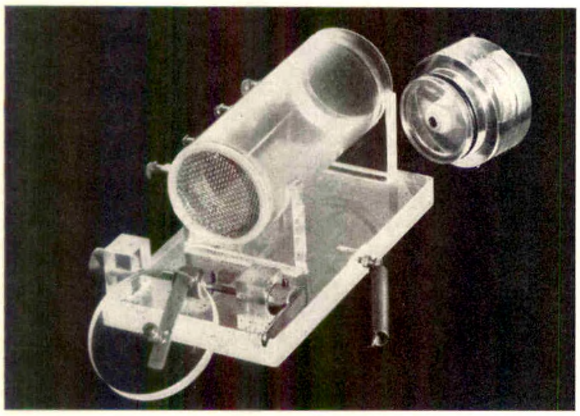

FIG. 1.

The plethysmograph shown with both ends open. The pressure transducer is located in the centre of the removable door at the far end. Wire mesh screen and a hinged door are at the opposite end allowing the chamber to be opened without releasing the mouse.

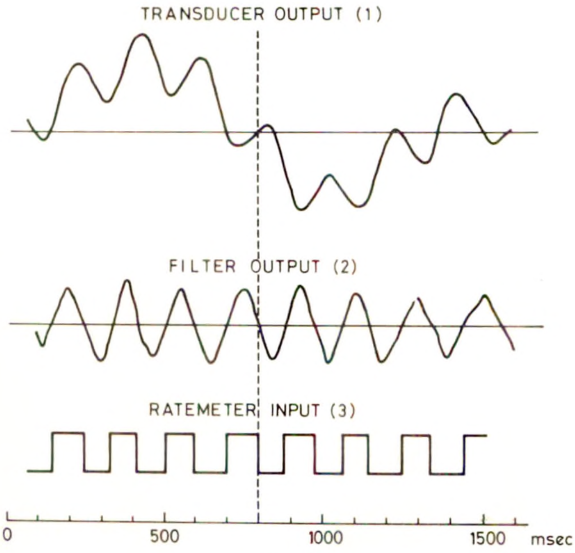

FIG. 2.

Typical waveforms obtained from the plethysmograph. The waveform numbers refer to various points in the circuit indicated in Fig. 3. The top trace (1) is a typical output from the transducer showing a slow component due to movement of the animal. In the filtered output (2) only the fast component ($\sim$5 Hz) is present. This signal was converted to a pulse waveform by the zero-crossing detector (3) suitable for frequency measurement.

A diagram of the modified transducer and electronic processing equipment is shown in Fig. 3. This system provides a simultaneous record of the rate and amplitude of pressure changes in the chamber which were due to the respiration of the mouse. The rate signal was calibrated with an oscillator in 1 Hz increments from 1 to 10 Hz, enabling the reading on the chart paper to be converted to Hz which corresponded to breaths per second. The amplitude signal was not calibrated and its magnitude was recorded directly in chart units.

Testing procedure

All mice were allowed to settle in the chamber for $\frac{1}{2}$ to 1 min before the ends were closed and measurements recorded. However, after the mice had been in the chamber several times, the settling period was less than $\frac{1}{2}$ min. At no time did the mice appear stressed in the chamber and they voluntarily entered the chamber with no assistance after several experiences in the chamber.

Continuous measurements were made for two min after closing the chamber. If sufficient data had not been obtained in this time air was allowed to enter the chamber and the measurements were repeated. It was often necessary to repeat the measurements before the mice became accustomed to the chamber; after this time the data were obtained in the first testing period. The average of the resting data for both parameters was read from the trace between 1 and 2 min of testing. A minimum period of 15 sec was regarded as a reliable trace and usually much more than this was obtained in the testing period.

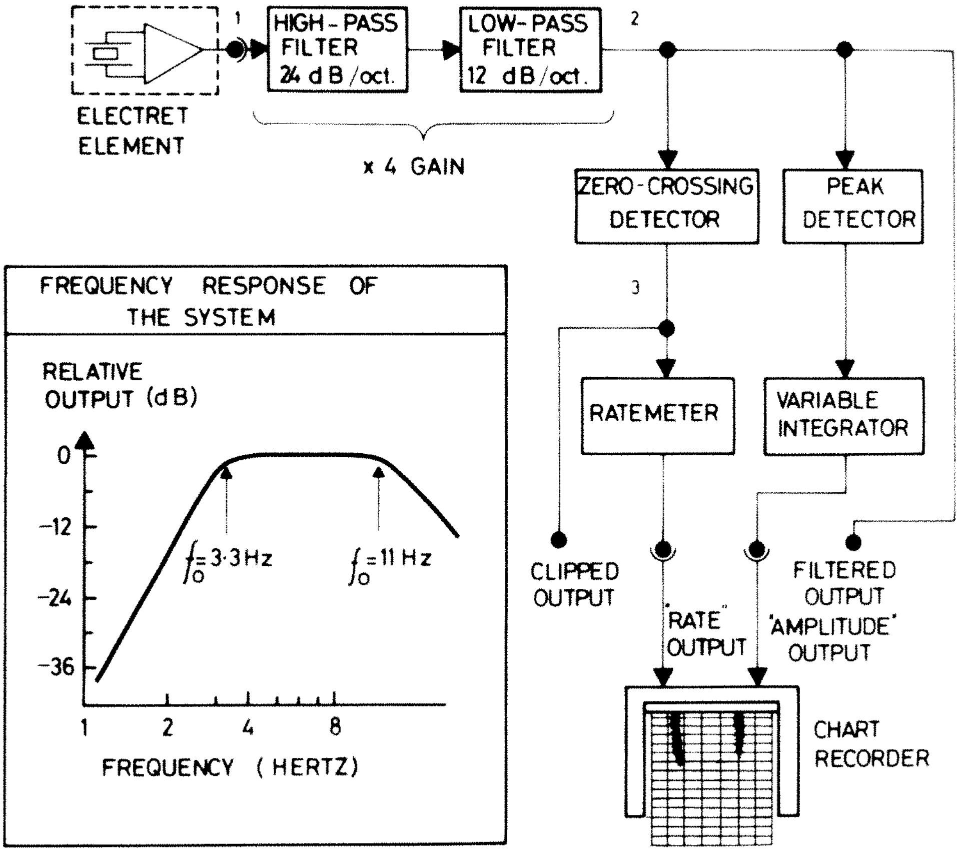

FIG. 3.

Block diagram of processing electronics. The filters were of the Sallen and Key configuration, Butterworth response (Tobey *et al.*, 1971); their frequency response is shown in the bottom left. The peak detector was a precision half-wave rectifier circuit followed by a variable time-constant integrator (20 ms–1 s). The rate-meter was based on a diode-transistor pump circuit (Anderson, 1972) with the output time constant also variable (100 ms–1 s). Typical output levels were ~100 mV on the amplitude output and 70 mV Hz^{-1} on the rate output. The clipped output could be fed to an external ratemeter. The numbers 1, 2 and 3 refer to the waveforms in Fig. 2.

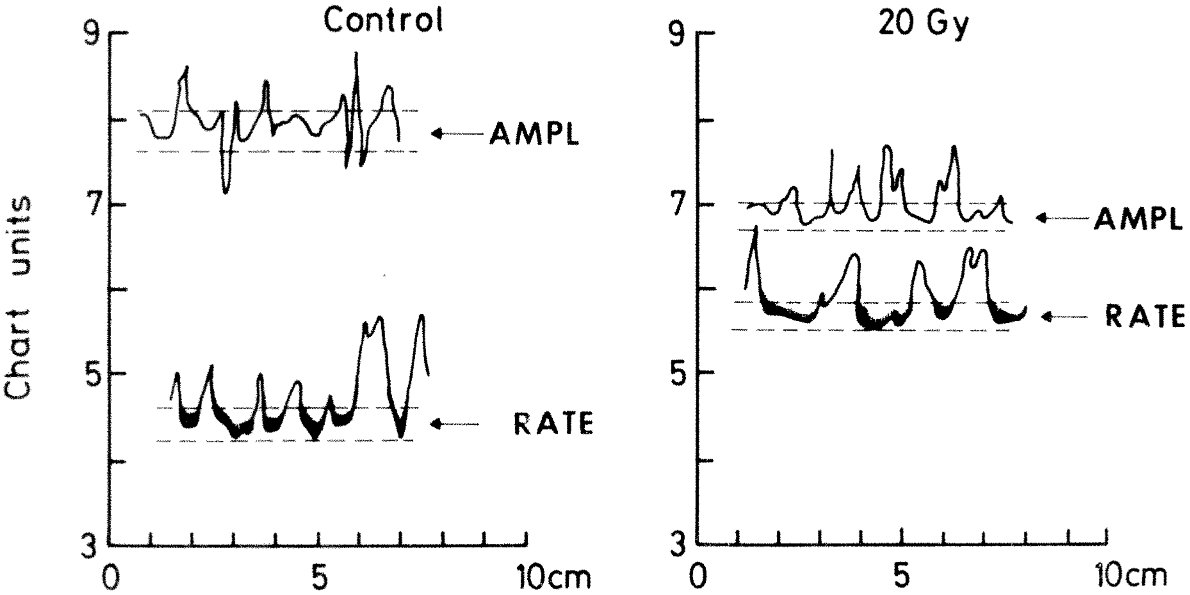

FIG. 4.

Pen recorder tracings from a sham irradiated mouse and a mouse given 20 Gy to both lungs. Testing time was 16 weeks after irradiation. The upper tracings represent the amplitude of pressure changes in the chamber, the lower the rate of pressure changes. The area between the dotted lines on each trace indicates the range of resting values from which the mean was calculated. The peaks represent animal movement which could not be electronically removed. Amplitude data were recorded in arbitrary chart units as indicated; the rate data were converted to Hz which corresponded to breaths per second. All rate data were expressed in breaths per minute. In this example, the rate of breathing was 330 (4.3 chart units) and 480 (5.8 chart units) breaths per minute for the control and irradiated mice respectively. The traces represent a time of 1.5 min; chart speed was 5 cm per min (bottom axis).

RESULTS

An example of the raw data from the chart recorder is shown in Fig. 4 for a sham-irradiated mouse and for a mouse tested at 16 weeks after 20 Gy. The lower trace represents the rate and the upper the amplitude. Some animal motion produced unwanted signals which were in the frequency range of interest. Because it was not feasible to eliminate these signals, fluctuations are apparent in the traces of both signals. The operator marked the trace to indicate when a mouse was at rest, so that spurious fluctuations were not incorporated into the data analysis. In this example the rates of breathing were 330 and 480 breaths per min for the control and irradiated mice respectively, *i.e.* 5.5 and 8.0 Hz. The amplitudes were 7.9 and 6.9 arbitrary units respectively. It is clear that significant changes occur in both of these functional parameters after irradiation.

The breathing rate of unanaesthetized sham-irradiated CBA mice varied from 321 to 350 breaths per min (±4%) between 9 am and 5 pm on five consecutive days. A larger variation was seen from three to nine months in this same group, ranging from 300 to 350 breaths per min (±8%). These variations did not appear to reflect a trend due either to a diurnal or an age related change. At 16 weeks after irradiation the breathing rate progressively increased after doses to both lungs greater than 11 Gy as shown in Fig. 5. Although the breathing rate of mice given only 11 Gy to both lungs exhibited a slight increase, this increase was not significant compared to the controls. A dose of 8 Gy produced no change in rate. The results from two separate experiments are plotted in Fig. 5. There were no significant differences in breathing rate between the two experiments in any dose group.

The amplitude exhibited the opposite dose-dependent pattern to the rate, decreasing with increasing dose, *i.e.* breathing became more shallow as it became faster (Fig. 6). Dose-effect curves were again obtained with a threshold at 11 Gy. Dose-response curves from the second experiment exhibited the same pattern as the first although there was more scatter in the data. In addition, there were significant differences between the two experiments at two points, control and 8 Gy. During measurement of the 8 Gy group at 16 weeks it was found that clamping the end door more tightly caused a 10% increase in the amplitude reading. Subsequently, a stronger spring and new O-ring seal around the door

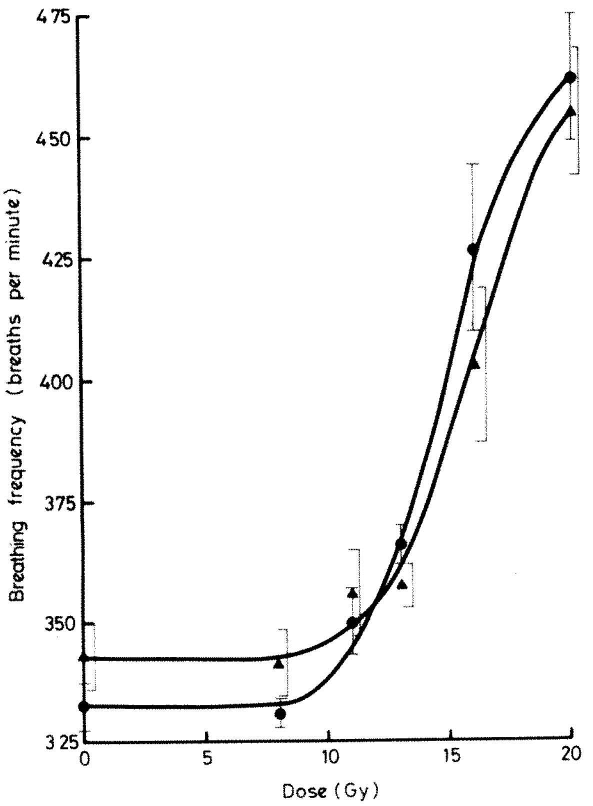

FIG. 5.

Breathing frequency as a function of radiation dose at 16 weeks after irradiation, showing a progressive increase in rate with dose with a threshold at 11 Gy. The results from two experiments are plotted; there was no significant difference in breathing rate at any dose between the two experiments. Each dose point represents the mean of 10 mice in one experiment (●) and 7 in the other (▲). Error bars are 1 SEM.

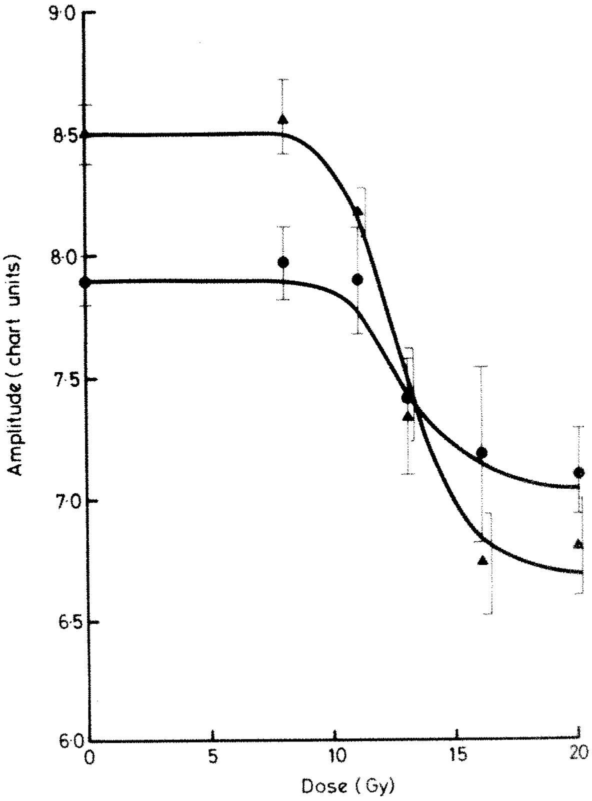

FIG. 6.

Amplitude of breathing at 16 weeks after graded X-ray doses to both lungs, showing a reduction with increasing dose. Data are from the same mice for which breathing rate is plotted in Fig. 5; the symbols correspond to the two experiments plotted in Fig. 5. Error bars represent 1 SEM. Significant differences are evident in the sham and 8 Gy group between the two experiments; a minor air leak found in the chamber probably contributed to these differences.

were introduced. In addition, the amplitude signal was routinely checked by testing the same control mouse as a "standard" before testing the experimental groups; *i.e.* several times per day. If his amplitude had changed significantly, the system was checked for air leaks or electronics problems and rectified before further use. This occurred at intervals of a few months when the O-ring seal became deformed.

DISCUSSION

Total body plethysmography is often used to measure pulmonary function in human subjects (Bedell *et al.*, 1956; Comroe *et al.*, 1959; Du Bois, 1959; Du Bois *et al.*, 1956a; Schmidt and Cohn, 1961). Two parameters of lung function in mice were simultaneously monitored in this study, respiration rate and pressure amplitude. The ratemeter output was accurately converted to breaths per min by calibrating the equipment with an oscillator. The mean breathing frequency of 328 breaths per min in control mice is higher than previously reported values for mice, 160 and 190 breaths per min with ranges of 60–230 and 97–123 respectively (Spector, 1956; Crosfill and Widdicombe, 1961). However, breathing frequency is strain dependent and often sex dependent, factors which were not reported in the previous studies (Travis *et al.*, in preparation). Another factor which might be expected to increase breathing rate is stress. Subjectively the mice appeared unstressed in the chamber. Further experiments have also shown that breathing rate is decreased rather than increased as a result of swimming stress. These findings suggest that the higher rates measured in this study were not due to stress. Because of the discrepancy between our value for breathing frequency and those previously reported, the value reported in this study has been confirmed by two other methods, one visually by high speed filming and one using a recording stethoscope. The latter simultaneously measured heart rate, which was approximately 2–3 times higher than the breathing rate.

The amplitude signal, which was not calibrated, was subject to more technical problems than the rate signal. It was affected by small movements of the mouse and, although the signal was filtered to eliminate large movements, it was not feasible to eliminate all movement in the frequency range of interest. Therefore, mean values were more difficult to obtain for breathing amplitude than for rate. The amplitude signal was also affected by temperature and humidity changes after the mouse had been in the closed chamber for more than two min. An increase in either of these factors would cause an increase in pressure, therefore temperature and humidity were controlled by opening the chamber every two min during testing of an animal. This introduction of fresh air also eliminated the potential problem of O_2 depletion and CO_2 accumulation in the closed chamber, changes which in themselves would affect breathing frequency and depth. Because the rate and amplitude of breathing were continuously recorded when a mouse was in the closed chamber, sudden changes in either signal were immediately visible on the chart paper. Few significant changes were observed in either trace during the two min of testing in any group of mice, irradiated or control, suggesting that the amount of O_2 depleted and CO_2 accumulated in this time had no significant effect. In a few traces a gradual small increase (of 5 to 10%) in rate was seen over the two min period, which may have been due to the increase in CO_2 content. The value then used was the mean of the rate before and after the increase.

Appendix 1 shows that the effect of CO_2 accumulation would be expected to be possibly just significant.

These observations are consistent with calculation of gas composition changes in the chamber based on the known rate of exchange of O_2 and CO_2 in normal human subjects. Applying these figures to mice having a respiration rate of 328 breaths per min, 1.13% of the available O_2 is converted to CO_2 in 1 min, 2.2% in 2 min and 3.2% in 3 min (Appendix 1). The amount of O_2 depleted and CO_2 accumulated in 2 min would not cause changes in either functional parameter, as was indeed observed experimentally.

Although lung gas volume and airway resistance in patients can be calculated from plethysmographic measurements (Du Bois *et al.*, 1956a; Du Bois *et al.*, 1956b; Bedell *et al.*, 1956), the amplitude results in the present study are more difficult to interpret. The amplitude of the pressure signal is related to four lung parameters: airway resistance, ventilation, lung volume and the shape of the breathing cycle. A reduction in any one or combination of these four would cause a reduction in the amplitude of the pressure change.

It is unlikely that airway resistance is decreased. Rather, airway resistance would be *increased* if fibrosis were occurring, a histological change which has not been observed at 16 weeks in any of the dose groups. Although a change in airway resistance cannot be excluded, this parameter is the least likely contributor to the reduced amplitude observed.

A more probable factor influencing amplitude is the shape of the breathing cycle. Normally the breathing cycle consists of a slow intake of air during inspiration followed by a rapid exhalation of air during expiration. One method of compensating for respiratory insufficiency is to optimize the breathing cycle to equal periods of steady flow during inspiration and expiration, thereby effectively reducing the amplitude of the pressure change in the plethysmograph.

The most probable lung parameters reducing breathing amplitude in the present study are a reduction in lung volume and ventilation. Decreased ventilation has been observed in dog lungs at 16 weeks after irradiation, the time when amplitude was reduced in the present study (Teates, 1965). In both studies, this functional change occurred before histological evidence of fibrosis and during severe diffuse pulmonary oedema. The latter pathological change could cause a decrease in both lung volume and ventilation.

In the present study, the amplitude signal represents a complex of pulmonary functional parameters in the mouse but undoubtedly reflects the depth of breathing. Although none of the four functional parameters affecting amplitude can be isolated in the system used, it is reasonable to assume that the magnitude of change in any of these parameters would be constant within a group of mice receiving a specific dose. In addition, the relative contribution of each of these factors is not important for a dose-response curve, provided that each does depend upon the dose.

Both rate and depth of breathing yield clear dose-response relationships at 16 weeks. A threshold dose of 11 Gy was observed for both effects. The dose response curves show a mirror image relationship of the two parameters, respiration rate increasing while the depth of breathing proportionally decreased. At this post-irradiation time, the shapes of the two curves are not significantly different and may reflect the same pathological change. Rapid shallow breathing indicates a reduction in lung compliance. This breathing pattern effectively reduces the increased work of breathing resulting from stiffening of the lungs. Although decreased compliance is usually associated with fibrosis, rapid, shallow breathing was observed before the onset of fibrosis and during severe pulmonary oedema (Travis *et al.*, 1978). A reduction in lung compliance has been reported during the oedematous phase of the radiation response in rat and dog lungs (Shrivastava *et al.*, 1974). The doses used were similar to those used in the present study. It is likely that the rapid, shallow breathing pattern observed may be a compensatory response to decreased lung compliance due to oedema, the latter causing a concomitant reduction in lung volume, one of the factors which affect amplitude. Further investigations are being conducted to measure pulmonary compliance.

If the relationship between breathing rate and depth observed at 16 weeks is true at other times after irradiation, it may be feasible to assess routinely only one of these parameters. Because the amplitude signal cannot be calibrated absolutely in the present system and because there are more fluctuations and scatter in the amplitude than in the breathing rate, the latter is the parameter of choice.

The present tests indicate changes in rate and depth of breathing at earlier times and after lower doses than those used when death is the endpoint (Field and Hornsey, 1974; Hornsey *et al.*, 1975; Phillips and Margolis, 1972; Steel *et al.*, 1978). CBA mice exposed to 13 Gy to the whole thorax, a dose within the reported range of LD_{50} values for pulmonary lethality in other strains, have all survived 36 months (Travis *et al.*, unpublished). The rate and depth of breathing had, however, changed significantly from control values by 16 weeks after 13 Gy. All mice given 16 Gy or higher doses were killed between 15 and 20 weeks after irradiation because of respiratory distress, but significant changes in rate and depth of breathing were recorded for at least six weeks before killing.

These functional changes therefore provide a useful new method for assessing pulmonary response of mice to radiation. The technique described not only responds at lower doses than LD_{50} and is non-non-invasive, but is also a quantitative method.

ACKNOWLEDGMENTS

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APPENDIX 1

The following equations were used to calculate O_2 depletion and CO_2 production in the chamber after various periods of respiration.

Equation 1. O_2 depletion

$$n_z\,(O_2) = n_0\,(O_2)\left[1 - \left(\frac{V_T}{V_c}\,[1 - f]\right)\right]^Z$$

Where:

Z = number of breaths
$n_z\,(O_2)$ = amount of O_2 or CO_2 in chamber after Z breaths
n_0 = amount of O_2 or CO_2 in chamber at $Z = 0$
V_T = tidal volume (volume of air exhaled) by a mouse ($0.08\ cm^3$, eq. 2 and 3)
V_c = volume of chamber less the volume of the mouse ($95\ cm^3$)
f = ratio of exhaled to inhaled O_2 (16%/20%)

Equation 2. Calculation of V_T

$$V_T = \frac{\text{Minute volume (cm}^3\text{ air/min—Eq. 3)}}{\text{Breathing frequency (mean observed value)}}$$

$$= \frac{26.9\ \text{cm}^3/\text{min}}{328\ \text{breaths/min}}$$

$$V_T = 0.08\ \text{cm}^3/\text{breath}$$

Equation 3. Calculation of minute volume (Guyton, 1947).
Minute volume $= 2.10 \times \text{wt (gm)}^{0.75}$
Minute volume $= 26.9\ cm^3$ for a 30 gm mouse

Substituting in Eq. 1 and calculating vol. % of O_2 and CO_2 in chamber

Z	t (minutes)	n_z/n_0	Vol. %O_2	Vol. %CO_2
0	0	1	20.99	0.03
1	0.003	0.9998		
330	1	0.9461	19.86	1.13
660	2	0.8950	18.79	2.20
990	3	0.8468	17.77	3.22
1650	5	0.7579	15.91	5.08

Breathing rate would be expected to increase when 3 to 5% of CO_2 had been accumulated. Even if the above times should be shortened by a factor of two, because the normal breathing rates of our mice were faster than those in the literature, no increase in rate due to CO_2 would be expected until near the end of our test period. In practice the traces were flat between 1 and 2 min when the values were read off the chart.

REFERENCES

ANDERSON, D., 1972. Linear frequency meter. *Wireless World*, *78*, 38–40.

BEDELL, G. N., MARSHALL, R., DU BOIS, A. B., and COMROE, J. H., JR., 1956. Plethysmographic determination of the volume of gas trapped in the lungs. *Journal of Clinical Investigation*, *35*, 664–670.

CHAUSER, B. M., HUDSON, F. R., and LAW, M. P., 1976. Renal function in the rat following irradiation. *Radiation Research*, *67*, 86–97.

COMROE, J. H., JR., BOTELHO, S. Y., and DU BOIS, A. B., 1959. Design of a body plethysmograph for studying cardiopulmonary physiology. *Journal of Applied Physiology*, *14*, 439–444.

CROSFILL, M. L., and WIDDICOMBE, J. G., 1961. Physical characteristics of the chest and lungs and the work of breathing in different mammalian species. *Journal of Physiology, 158*, 1–14.

DU BOIS, A. B., 1959. New concepts in cardiopulmonary physiology developed by the use of the body plethysmograph. *The Physiologist, 2*, 8–24.

DU BOIS, A. B., BOTELHO, S. Y., BEDELL, G. N., MARSHALL, R., and COMROE, J. H., JR., 1956a. A rapid plethysmographic method for measuring thoracic gas volume: a comparison with a nitrogen wash-out method for measuring functional residual capacity in normal subjects. *Journal of Clinical Investigation, 35*, 322–326.

DU BOIS, A. B., BOTELHO, S. Y., and COMROE, J. H., JR., 1956b. A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *Journal of Clinical Investigation, 35*, 327–335.

FIELD, S. B., and HORNSEY, S., 1974. Damage to mouse lung with neutrons and X rays. *European Journal of Cancer, 10*, 621–627.

FRAIM, F., and MURPHY, R., 1970. Miniature electret microphone. *Journal of the Audio Engineering Society, 18*, 32–36.

GLATSTEIN, E., BROWN, R. C., ZANELLI, G. D., and FOWLER, J. F., 1975. The uptake of rubidium 86 in mouse lungs irradiated with fractionated doses of X rays. *Radiation Research, 61*, 417–426.

GUYTON, A. C., 1947. Measurement of the respiratory volumes of laboratory animals. *American Journal of Physiology, 150*, 70–77.

HAYASHI, S., and SUIT, H. D., 1971. Effect of fractionation of radiation dose on callus formation at site of fracture. *Radiology, 101*, 181–186.

HIRST, D. G., DENEKAMP, J., and TRAVIS, E. L., 1977. Vascular changes in the mouse mesentery after single doses of radiation. *International Journal of Radiation Biology, 32*, 384–385.

HOPEWELL, J. W., 1975. Early and late changes in the functional vascularity of the hamster cheek pouch after local X irradiation. *Radiation Research, 63*, 157–164.

HORNSEY, S., KUTSUTANI, Y., and FIELD, S. B., 1975. Damage to mouse lungs with fractionated neutrons and X rays. *Radiology, 116*, 171–174.

PHILLIPS, T. L., and MARGOLIS, L. W., 1972. Radiation pathology and the clinical response of lung and oesophagus. In *Frontiers of Radiation Therapy and Oncology*, ed. J. M. Vaeth, vol. 6, pp. 254–273 (University Park Press, Maryland).

SCHMIDT, A. M., and COHN, J. E., 1961. Modified body plethysmography for study of cardiopulmonary physiology. *Journal of Applied Physiology, 16*, 935–937.

SHRIVASTAVA, P. N., HANS, L., and CONCANNON, J. P., 1974. Changes in pulmonary compliance and production of fibrosis in X irradiated lungs of rats. *Radiology, 112*, 439–440.

SPECTOR, W. S., 1956. *Handbook of Biological Data*, p. 267 (W. B. Saunders, Philadelphia).

STEEL, G. G., ADAMS, K., and PECKHAM, M. J., 1978. Lung damage in C57BL mice following combined chemotherapy and thoracic irradiation. (Abstract). *British Journal of Radiology, 51*, 239.

STEWART, F. A., 1977. Radiation response of mouse urinary bladder. *International Journal of Radiation Biology, 32*, 385.

TEATES, C. D., 1965. Effects of unilateral thoracic irradiation on lung function. *Journal of Applied Physiology, 20*, 628–636.

TOBEY, G. E., GRAEME, J. G., and HUELSMAN, L. P., 1971. *Operational Amplifiers*, pp. 282–327 (McGraw Hill, New York).

TRAVIS, E. L., VOJNOVIC, B., HIRST, D. G., and HILL, S. A., 1978. Quantitative changes in rodent lungs after irradiation. (Abstract). *British Journal of Radiology, 51*, 239.

VAN DER KOGEL, A. J., SISSINGH, H. A., and ZOETELIEF, J., 1977. Effects of fractionated irradiation with 300 kV X rays and 15 MeV neutrons on the rat spinal cord. *International Journal of Radiation Biology, 32*, 389.

VATISTAS, S., and HORNSEY, S., 1966. Radiation induced protein loss in the gastrointestinal tract. *British Journal of Radiology, 39*, 547–550.

WHITE, A., and HORNSEY, S., 1977. Dose fractionation studies in rat spinal cord. *International Journal of Radiation Biology, 32*, 383.

WITHERS, H. R., 1967. Recovery and repopulation *in vivo* by mouse skin epithelial cells during fractionated irradiation. *Radiation Research, 32*, 227–239.

WITHERS, H. R., and ELKIND, M. M., 1969. Radiosensitivity and fractionation response of crypt cells of mouse jejunum. *Radiation Research, 38*, 598–613.

1979, *British Journal of Radiology*, 52, 75–77 JANUARY 1979

Technical note

Use of thermoluminescent dosimeters for measuring dose distribution with high spatial resolution in partial-body irradiation of small animals

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During the last few years partial-body irradiation techniques have become more extensively used in several types of radiobiological experiments, such as studies of the radiosensitivity of individual organs and tumours, studies on the carcinogenic action of collimated radiation beams, etc.

Such techniques entail the use of lead shields of various shapes, in order to achieve the best approximation to the ideal of zero-dose in the shielded tissues. Unfortunately, scattered radiation coming from the adjacent unshielded parts of the body cannot be prevented from reaching the shielded regions and giving there a more or less significant dose.

In order to undertake a detailed study of the resulting dose distribution in small animals such as mice, dosimeters with a very high spatial resolution are required. Thermoluminescent dosimeters (TLD) are very useful devices in this respect. Modern sintered TLDs (either pure or Teflon-mixed) are quite small and easy to handle. Some of them, such as LiF and BeO, are also tissue-equivalent, with an almost flat energy-response curve; this characteristic greatly reduces the need for correction factors to account for the change in quality of scattered radiation compared to primary radiation (Puite and Crebolder, 1974; Scarpa *et al.*, 1975).

Papers on the use of TL dosimeters in partial-body irradiations of small animals have recently been published by Bojtor *et al.* (1974; 1977). The present contribution is a brief description of the technique with results of a dosimetric study carried out in two practical cases of partial-body irradiation of mice.

EXAMPLES OF PRACTICAL APPLICATION

The first case is an open-beam irradiation with shielding of a hind leg.

The aim of the experiment was to sterilize completely the stem cell compartment of the hemo-lympho- and immuno-poietic systems of the mouse, but to save part of the same system for later irradiation with a defined radiation dose.

As shown in the insert of Fig. 1, the hind limb was simulated by a polythene tube (7.8 mm external diameter, 45 mm long) and shielded with an open-ended, 3 mm-thick, hemicylindrical lead tunnel resting on a lead platform of the same thickness. Several dosimeters were located in a row inside this leg phantom. As dosimeters square LiF chips were used (Victoreen ^{N}LiF) with dimensions 3.2 × 3.2 × 0.7 mm, the specific gravity being 2.4 g/cm^3. An average density around unity was obtained by spacing the dosimeters with 1 mm thick Styrofoam discs.

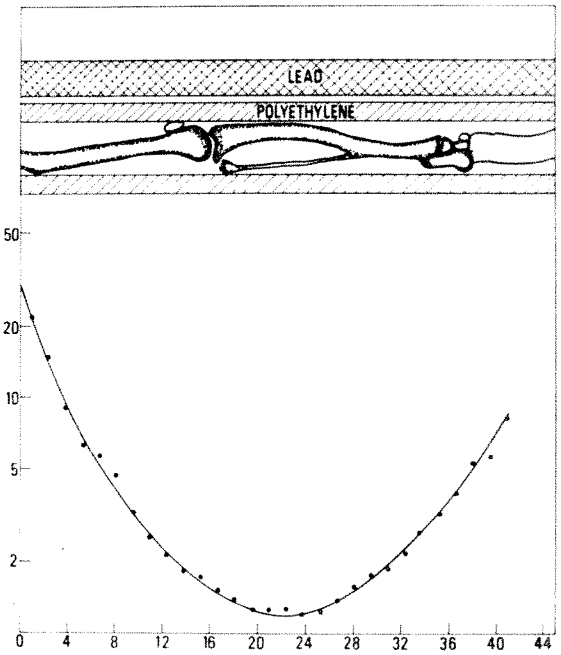

FIG. 1.

Dose distribution along a shielded hind limb of a mouse. Anatomical points of reference (the bones of the leg, not actually present during the dosimetric measurements) and a longitudinal section of the leg phantom and shield are shown in the insert.

The rest of the body of the mouse was simulated with a PMMA (Perspex) phantom (the same as used in experiment 2 and shown in Fig. 3), in which other LiF dosimeters were positioned to evaluate the dose to unshielded parts: this dose was used as a reference.

The irradiation was carried out using an uncollimated, vertical beam, whose uniformity was within ±5% in the area to be occupied by the animals.

The relative dose distribution along the shielded hind limb is illustrated in the graph of Fig. 1. The minimum dose is, obviously, in the central part of the shield, while the dose increases rather quickly near the two ends, due to scattered radiation. It follows that the role of primary radiation passing through the lead shield is almost negligible, except in the proximal half of tibia and fibula; in fact, the theoretical transmission of the X rays used in this study (250 kV, 0.5 mm Cu total filtration) through a 3 mm-thick lead shield was calculated to be about 0.6%, using Kramers' theory for evaluating the spectral distribution of the filtered beam.

It should be pointed out that the rising portion of the curve at distances above 25 mm could presumably have been eliminated if the lead shield had been extended to the right beyond the limit of the beam. The distinct asymmetry of the curve is readily explained by the fact that most of the scattered radiation comes from the mouse body (left side of the figure).

A second series of dosimetric studies is concerned with irradiation of half the mouse thorax, in the context of experiments on induction of lung cancer.

Ten mice were placed on a lead platform (*i.e.* a thick support giving minimum back-scattering) in a radial arrangement, heads towards the central axis. Most of the body of each mouse was covered by a 4 mm-thick, half-cylindrical lead shield, in which a trapezoidal window allowed only one of the lungs to be irradiated. The dimensions of this window were:

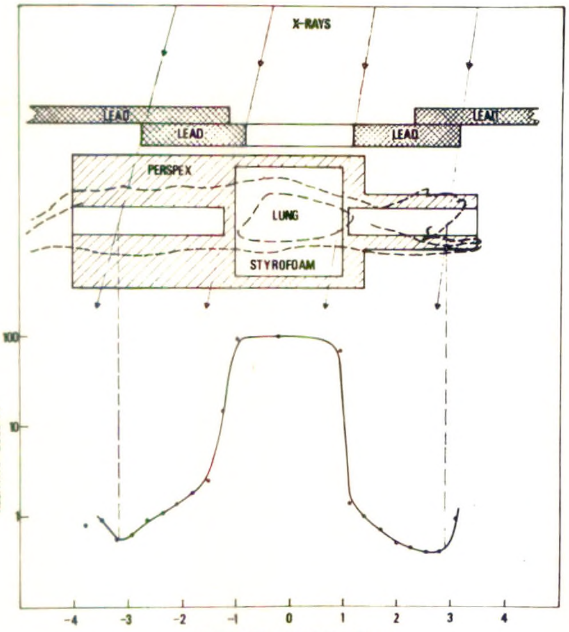

FIG. 2.

Dose distribution along the central axis of the body of a mouse irradiated in the thoracic region (see text). Insert: longitudinal section of the mouse phantom and of the lead shields.

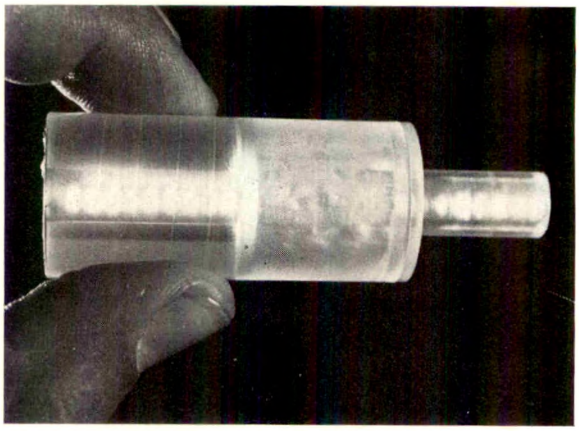

FIG. 3.

Mouse phantom used for studying the distribution of dose in collimated lung irradiations.

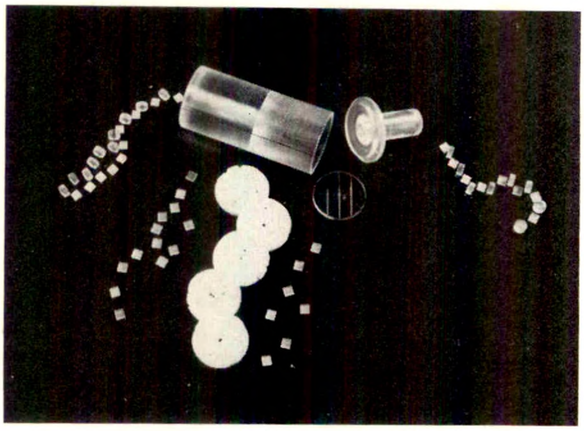

FIG. 4.

Exploded view of the phantom, with all dosimeters and spacers used in each experiment.

major base 10 mm, minor base 4 mm, altitude 20 mm. Two more, partially overlapping, lead shields completed the protection of each mouse from primary radiation, as can be seen in the insert of Fig. 2.

The mouse phantom used for this study is shown in Fig. 3 and its longitudinal section in the insert of Fig. 2. Dosimeters were again LiF chips, 3.2 × 3.2 × 0.7 mm, individually calibrated and located 2.8 mm apart in the central channels (head and abdomen) and in the thoracic cavity of the phantom. The low density of lung tissue (around 0.2, according to unpublished evaluations by Scarpa and Moscati) was simulated by using Styrofoam spacers. Figure 4 shows an exploded view of the phantom, with all dosimeters and spacers.

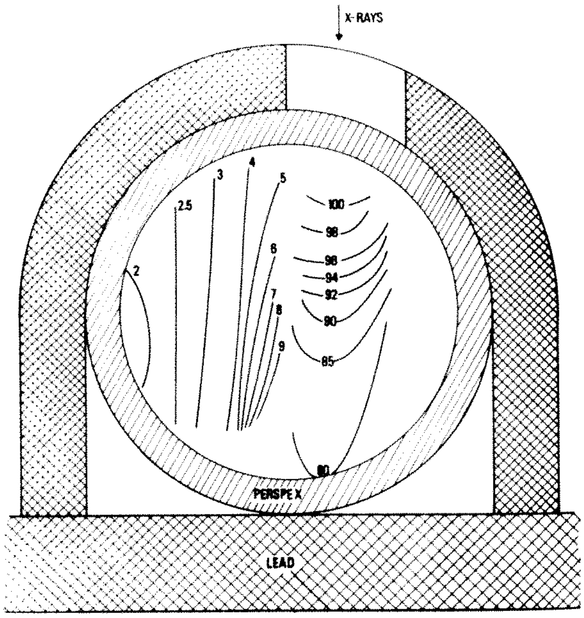

Fig. 5.

Dose distribution in the cross section of the mouse thorax. Inside diameter of the Perspex tube: 20 mm. Width of the window in the shield: 7 mm.

The results of this experiment are plotted in Fig. 2. The relative dose drops quickly from thorax to abdomen and head, reaching very low values around 0.5% (theoretical transmission through 4 mm lead: 0.2%). The slight—but well beyond experimental error—increase in dose towards both ends of the curve is due to the effect of overlapping of the shields (see insert) on the primary radiation.

An attempt was also made to study the dose distribution across the irradiated hemithorax. The thoracic cavity of the mouse phantom (diameter: 20 mm) was filled with nine very thin Styrofoam layers placed parallel to the beam direction; 34 dosimeters were then placed between the layers, in order to obtain a regular set of measuring points.

The results of this experiment are shown in Fig. 5; the isodose curves were derived by graphical interpolation of the experimental data. The high gradient of dose in the central region (mediastinum) is well demonstrated. The opposite lung receives a very low dose (2 to 4%), with the exception of its lower part where a significant increase in dose is apparent, probably due to back-scattering from the underlying materials.

Acknowledgments

The authors would like to express their gratitude to Professor J. F. Fowler, Gray Laboratory, Mount Vernon Hospital, and to Mr. J. A. Dennis, NRPB, Harwell, for their valuable advice and encouragement.

REFERENCES

Bojtor, I., Hiesche, K., and Schnell, P. O., 1974. Dose from scattered roentgen radiation to a protected part of a mouse phantom. *Acta Radiologica (Therapy, Physics, Biology)*, *13*, 32–36.

Bojtor, I., El-Mahdy, A. M., and Wakley, J., 1977. Dose to the shielded thymic region of irradiated mouse cadavers. *Acta Radiologica (Therapy, Physics, Biology)*, *16*, 361–367.

Puite, K. J., and Crebolder, D. L. J. M., 1974. Energy dependence of thermoluminescent dosimeters for X-ray dose and dose distribution measurements in a mouse phantom. *Physics in Medicine and Biology*, *19*, 341–346.

Scarpa, G., Moscati, M., and Roca, V., 1975. More data on the energy change of X-rays in a mouse phantom. *Physics in Medicine and Biology*, *20*, 321–322.

1979, *British Journal of Radiology*, *52*, 78–80

Case report

Abdominal aortic rupture simulating thoracic dissection

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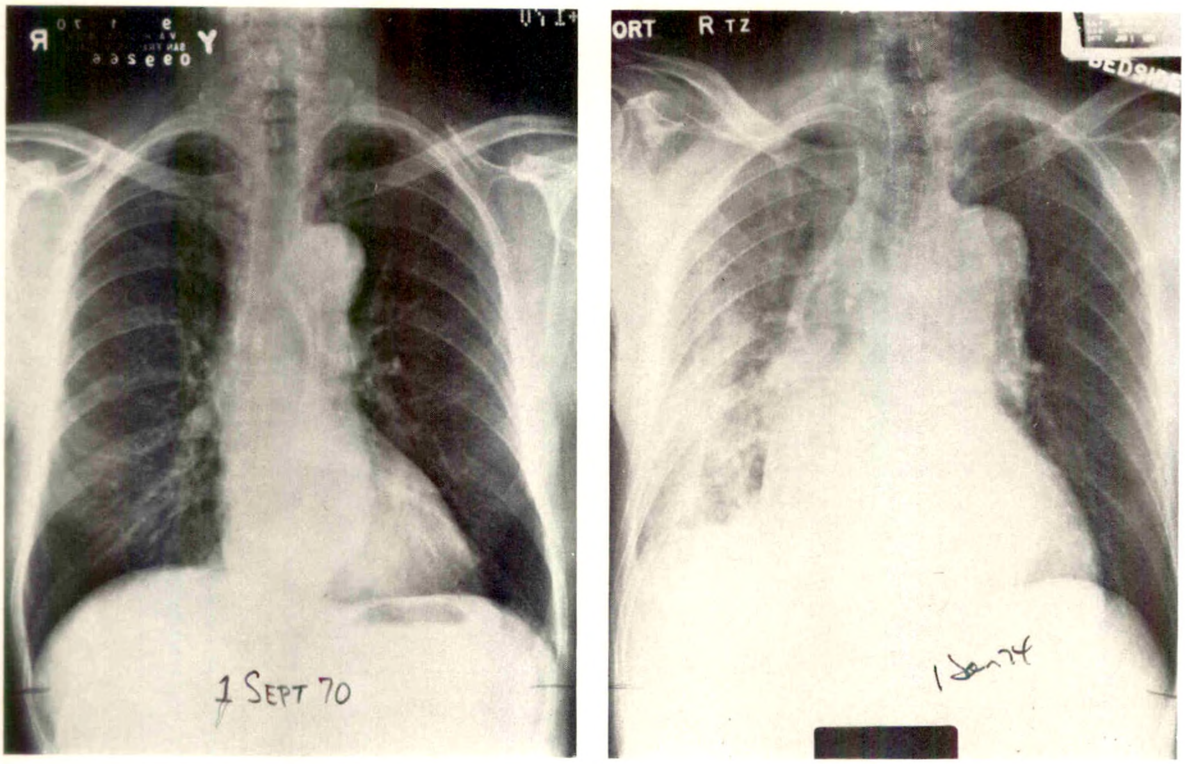
A rupture of the abdominal aorta can exhibit the clinical and radiographic findings of a thoracic dissection. We wish to stress the need for arteriographic assessment of the entire aorta when thoracic aortic dissection or rupture is suspected.

CASE REPORT

A 63-year-old man, six years after resection of an infrarenal aortic aneurysm and placement of an aorto-iliac Dacron by-pass graft, was hospitalized because of 36 hours of upper abdominal pain and chest pain radiating to the left shoulder. He had no measurable blood pressure and no palpable axillary or femoral pulses. With intravenous administration of fluid, pulses returned rapidly and blood pressure rose to 140/80. The patient's neck veins were distended. There was a grade I/VI systolic ejection murmur. The abdomen was soft and non-tender with no pulsation or palpable mass, and anal sphincter tone was absent. The patient was areflexic below the umbilicus.

Compared with a previous chest X-ray film (Fig. 1A) an A.P., portable chest X-ray film (Fig. 1B) revealed marked mediastinal widening and hydrothorax on the right.

Arch aortography (Fig. 2A and B) performed via the right femoral approach disclosed some narrowing of the descending thoracic aorta and a prominent soft-tissue mass adjacent to the descending aorta. No intercostal arteries could be identified above the level of T10. Except for tortuosity of the left subclavian artery, the aortic root, transverse aorta, and brachiocephalic vessels were normal. Because neither the lumen of a dissection nor a site of intimal tear was visible on the thoracic aortogram, an abdominal aortogram was obtained to attempt to demonstrate the re-entry site of the suspected dissection. An injection made at the level of the thoraco-abdominal junction (Fig. 3) revealed a ruptured



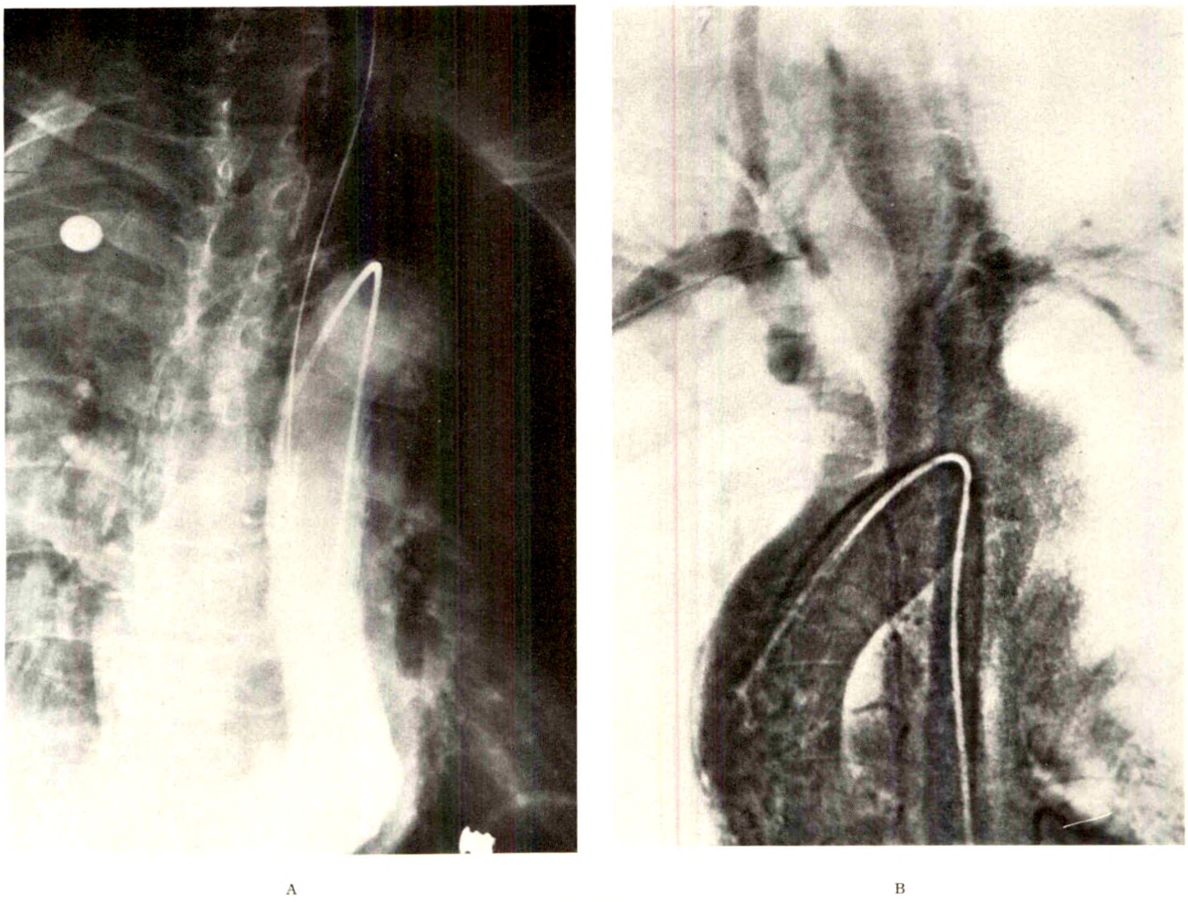
A

B

FIG. 1.

(A) Chest X-ray film obtained three years before admission.

(B) Admission chest X-ray film showing marked mediastinal widening and right hydrothorax.



A B

FIG. 2.

(A) Arch aortogram in the left posterior oblique projection demonstrating a para-aortic mass.

(B) Subtraction technique, right posterior oblique projection showing narrowing of the descending thoracic aorta.

suprarenal abdominal aortic aneurysm and a large retroperitoneal mass displacing the aorta to the left. Contrast medium extravasated from the right lateral aspect of the aneurysm.

Because of the location and extent of the lesion, surgery was not attempted; the patient died.

Post-mortem examination disclosed 2000 ml serosanguinous fluid in the right hemi-thorax. The thoracic aorta was tortuous and atherosclerotic. A 9×9×5 cm aneurysm occupied the abdominal aorta from just below the level of the diaphragm to the coeliac artery; a 3 mm perforation was present in the right lateral wall of the aneurysm. Via the perforation, the lumen of the aneurysm communicated with a partially organized haemorrhagic mass (approximately 2000 cc) in the retroperitoneum, which extended through a diaphragmatic rupture into the mediastinum. There was no dissecting aneurysm of the thoracic aorta.

DISCUSSION

The radiographic sign of thoracic dissection most frequently seen on the plain chest X-ray film is widening of the mediastinum, often with a para-aortic mass that is less dense than the aorta itself (Dow *et al.*, 1966; Dinsmore *et al.*, 1972). This sign may be unreliable (Price *et al.*, 1971); increase in aortic wall thickness can also be produced by fat, sclerosing aortitis, or neoplasm. In our patient the para-aortic mass was produced by blood that had entered the mediastinum from a ruptured abdominal aneurysm.

On a thoracic aortogram the finding most consistent with thoracic dissection is compression of the true lumen of the aorta (Dinsmore *et al.*, 1966; Shuford *et al.*, 1969). In our case this compression was produced by mediastinal haematoma. If thoracic dissection is suspected, it is of paramount importance to demonstrate not only compression of the true channel of the aorta but also the location of the intimal tear and re-entry site of the dissection (Stein and Steinberg, 1968; Soto *et al.*, 1972). Every attempt must be made to demonstrate the proximal

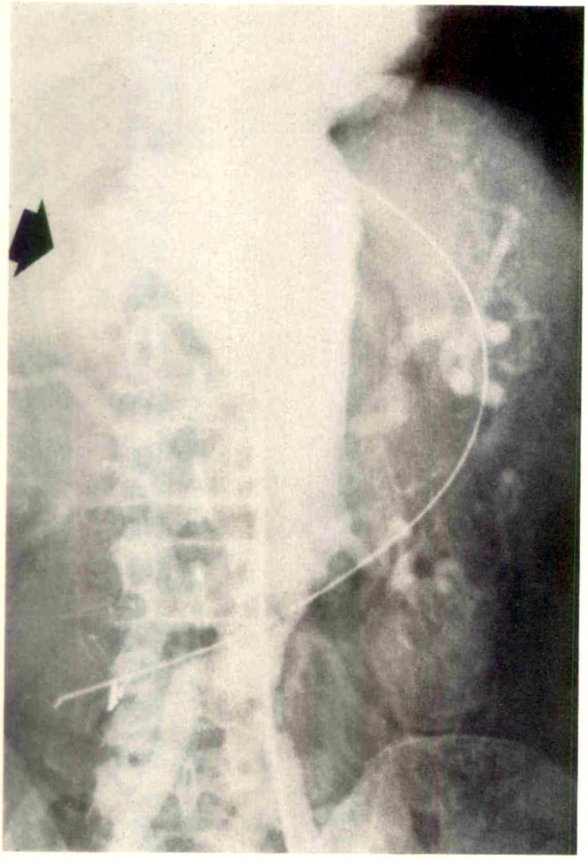


Fig. 3.

Abdominal aortogram demonstrating a suprarenal aortic aneurysm and displacement of the aorta to the left, consistent with a retroperitoneal mass. Contrast material extravasates (large arrow) from the right lateral aspect of the aneurysm.

and distal aspects of the intimal tear. The entire aorta should be examined. Our case shows that a retroperitoneal haematoma dissecting into the mediastinum can simulate a thoracic dissecting aneurysm. Although suprarenal aneurysms of the abdominal aorta, such as in our patient, are uncommon and have an extremely poor surgical prognosis (Graham *et al.*, 1968; Rainer *et al.*, 1973), dissection of blood into the mediastinum could also occur with rupture of an aneurysm located lower in the abdominal aorta, potentially a surgically reparable lesion. Steps taken to exclude thoracic dissecting aneurysm from the diagnosis will prevent an erroneous surgical approach.

REFERENCES

Dinsmore, R. E., Rourke, J. A., DeSanctis, R. D., Harthorne, J. W., and Austen, W. G., 1966. Angiographic findings in dissecting aortic aneurysm. *New England Journal of Medicine*, *275*, 1152–1156.

Dinsmore, R. E., Willerson, J. T., and Buckley, M. J., 1972. Dissecting aneurysm of the aorta: aortographic features affecting prognosis. *Radiology*, *105*, 567–572.

Dow, J., Roebuck, E. J., and Cole, F., 1966. Dissecting aneurysms of the aorta. *British Journal of Radiology*, *39*, 915–927.

Graham, A. L., Najafi, H., Dye, W. S., Javid, H., Hunter, J. A., and Julian, O. C., 1968. Ruptured aortic aneurysm. *Archives of Surgery*, *97*, 1024–1031.

Price, J. E., Gray, R. K., and Grollman, J. H. Jr., 1971. Aortic wall thickness as an unreliable sign in the diagnosis of dissecting aneurysm of the thoracic aorta. *American Journal of Roentgenology*, *113*, 710–712.

Rainer, W. G., Sadler, T. R., Jr., and Guillen, J., 1973. Ruptured abdominal aortic aneurysm: logistical and surgical considerations. *American Journal of Surgery*, *126*, 794–797.

Shuford, W. H., Sybers, R. G., and Weens, H. S., 1969. Problems in the aortographic diagnosis of dissecting aneurysm of the aorta. *New England Journal of Medicine*, *280*, 225–231.

Soto, B., Harman, M. A., Ceballos, R., and Barcia, A., 1972. Angiographic diagnosis of dissecting aneurysm of the aorta. *American Journal of Roentgenology*, *116*, 146–153.

Stein, H. L., and Steinberg, I., 1968. Selective aortography, the definitive technique, for diagnosis of dissecting aneurysm of the aorta. *American Journal of Roentgenology*, *102*, 333–348.

1979, *British Journal of Radiology*, *52*, 81–82 JANUARY 1979

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Report of a working party of the MCR isotope advisory panel on the application of the 10-day rule in radiopharmaceutical investigations

THE EDITOR—SIR,

We have followed the correspondence in the columns of *The British Journal of Radiology* with great interest (Ellis *et al.*, 1977, Croft and Maisey, 1978, Sear, 1978). There are many difficulties over implementing the ten-day recommendation in both radiology and nuclear medicine. The radiation doses involved in nuclear medicine diagnostic procedures are much smaller than those in radiology and the risks associated with them are very small indeed. Further, as indeed the working party point out, the ten-day recommendation cannot be applied to the use of radioisotopes with relatively long half lives.

In view of the correspondence on the subject we would suggest that the MRC isotope advisory panel reconsider their recommendation, taking more account of the practicability of applying it in the day to day diagnostic circumstances, where everyone agrees the clinical considerations are paramount.

We appreciate that there is a trend for increasing restrictions, but would ask the MRC panel to take a more realistic approach and state that the ten-day recommendation is not applicable to diagnostic radioisotope investigation.

Yours etc.,

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REFERENCES

CROFT, D. N., and MAISEY, M. N., 1978. Statements of the MRC isotope panel. *British Journal of Radiology*, *51*, 58–59.

ELLIS, R. E., NORDIN, B. E. C., TOTHILL, P., and VEALL, N., 1977. The application of the "ten-day rule" in radiopharmaceutical investigations. A report of the Working party of the M.R.C. Isotope Advisory Panel. *British Journal of Radiology*, *50*, 200–202.

SEAR, R., 1978. Applicability of the "ten-day rule" to radiopharmaceutical investigations. *British Journal of Radiology*, *51*, *59–60.*

The effect of high energy impurities on measurements of gamma-camera resolution and uniformity using ^{57}Co flood sources

THE EDITOR—SIR,

Commercially available ^{57}Co flood sources have small but important amounts of other cobalt isotopes present as impurities and it will be shown that these impurities can have a significant effect on gamma-camera resolution and uniformity measurements.

TABLE I

PHYSICAL DATA OF COBALT ISOTOPES

Isotope	Half-life	Principal γ-ray energies in MeV
^{56}Co	77d	0·51–36%; 0·845–100%; 1·24–66%
^{57}Co	270d	0·122–89%; 0·136–8%; 0·692–0·14%
^{58}Co	71d	0·51–30%; 0·81–101%
^{60}Co	5·26y	1·17–100%; 1·33–100%

The γ-ray energies and half-lives of the relevant cobalt isotopes are shown in Table I.

The main radioactive impurities present in a ^{57}Co flood source are ^{56}Co and ^{58}Co, and these isotopes produce γ rays with energies greater than 0·5 MeV and have half-lives of around 70 days. Thus a new ^{57}Co source will have a significantly higher proportion (typically up to 0·2%) of these high-energy isotopes than a source that is, say, one year old. The ^{60}Co impurity is initially present in much smaller amounts, but the proportion present will slowly increase and may become significant if the source is several years old.

A useful phantom for resolution checks is that designed by Anger (1973). This consists of a lead plate with sets of different diameter holes drilled in hexagonal arrays, the specified plate thickness being $\frac{1}{16}$ inch (1·6 mm). If an Anger phantom and a ^{57}Co flood source are placed on a gamma camera fitted with a collimator, some of the high energy γ-rays from the impurities will be Compton scattered in the lead plate, and a proportion of this scatter will appear in the energy "window" set around 122 keV. The ratio of the lead to hole areas in the Anger phantom is 17 to 1; thus, the scatter produced in the large area of lead from the high energy γ rays will add significantly to the ^{57}Co γ rays coming through the holes, even if the high energy γ rays are a small percentage of the total. The production of scatter in the collimator septa from the high energy photons will also lead to a marked loss of resolution and contrast in the system. It has been found with a new 5 mCi ^{57}Co flood source that even the 4 mm diameter hole pattern was barely visible when viewed on two modern gamma cameras (Elscint CE-1-7 with CCL3 collimator; Searle Pho-Gamma 1201 with 37 tube upgrade and LEAP collimator) whereas the 2 mm holes could be observed with a ^{99}Tc^{m} flood source. It was confirmed that this effect was not due to count-rate differences, by varying the amount of ^{99}Tc^{m} in the flood source between 2 mCi and 10 mCi.

As expected, the influence of the high energy impurities became less with time and after about 300 days the ^{57}Co flood source produced a well resolved image of the Anger phantom, although still inferior to that obtained with a ^{99}Tc^{m} flood source. This apparent improvement in the resolution with the aging of the ^{57}Co has now been observed in several ^{57}Co flood sources.

These effects were also observed with bar phantoms, although to a less pronounced degree, probably owing to the smaller area of lead in this type of phantom.

Field uniformity checks, which we also carry out with a collimator fitted, will also be influenced by the cobalt impurities. The scattered photons produced by the interaction of the high-energy γ rays with the collimator tend to smooth any non-uniformities present. In practice it has been found that the uniformities obtained using new ^{57}Co flood sources are consistently better than those obtained when using old ^{57}Co or ^{99}Tc^{m} flood sources. When using new ^{57}Co flood sources the average uniformity was $\pm 10\%$, whereas with old ^{57}Co and ^{99}Tc^{m} flood sources the average was $\pm 12\%$. These results were obtained with a variety of sources on a number of different occasions.

The age of the ^{57}Co flood sources may also account for the fact that differences between uniformities obtained with ^{57}Co and ^{99}Tc^{m} floods were observed by Hannan and Bessent (1974), and not observed by Jansson and Parker (1975).

We feel that it is desirable to carry out all routine checks with a collimator fitted to the camera, for the following reasons:

(1) the whole system is checked and any damage to the collimator is seen;
(2) the risk of damaging the vulnerable crystal is eliminated;
(3) time is saved in removing and replacing collimators.

It is apparent that care must be taken in using ^{57}Co flood sources to check the performance of the camera plus collimator system. An alternative commercial flood source employs ^{123}Te^{m}, with a principal gamma energy of 159 keV and a half-life of 120 days. When an Anger phantom was used to assess camera resolution the ^{123}Te^{m} flood source gave better results than ^{57}Co sources but slightly inferior results to those obtained using ^{99}Tc^{m}. The inferior performance of the ^{123}Te^{m} source is due to the presence of high-energy γ rays from other isotopes present (^{121}Te, ^{121}Te^{m}).

In conclusion, it would appear that the flood source of choice for the routine checking of gamma cameras is one employing ^{99}Tc^{m}. However, there are certain practical difficulties which should be considered. In addition to the inconvenience of using a liquid source of short half-life, a uniform distribution of activity must be achieved by adequate mixing and air bubbles should be avoided or be outside the camera's field of view. Also, if liquid sources are left filled for more than a few days, distortion can occur due to the absorption of water by the plastic material used in their construction.

Yours, etc.,
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Acknowledgment

The cobalt-57 and tellurium-123m flood sources were manufactured by The Radiochemical Centre, Amersham, and we wish to thank them for the loan of several sources.

REFERENCES

Anger, H. O., 1973. Testing the performance of scintillation cameras. Donner Laboratory and Lawrence Berkeley Laboratory Report no. LBL-2027.

Hannan, W. J. and Bessent, R. G., 1974. Pitfalls in gamma camera field uniformity correction. *British Journal of Radiology*, *47*, 820–821.

Jansson, L. G., and Parker, R. P., 1975. Pitfalls in gamma camera field uniformity correction. *British Journal of Radiology*, *48*, 408–409.

1979, *British Journal of Radiology*, *52*, 83–84 JANUARY 1979

Proceedings of The British Institute of Radiology

Comparison of diagnostic techniques for the chest and mediastinum

Abstracts of papers presented at a British Institute of Radiology meeting held on Thursday, March 16, 1978 at the Institute House, 32 Welbeck Street, London W1M 7PG

Regional ventilation and perfusion compared with the chest X-rays in pulmonary disease, by J. P. Lavender.
Computed tomography of the thorax, by L. Kreel
Is arteriography out of date? by I. H. Kerr
Lung imaging with radioactive aerosols, by F. Fazio

REGIONAL VENTILATION AND PERFUSION COMPARED WITH THE CHEST X-RAY IN PULMONARY DISEASE

By J. P. Lavender

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Images of regional perfusion by means of $^{99}Tc^{m}$ labelled particles have been available for a number of years but satisfactory comparative images of regional ventilation have only recently been developed. The use of the short-lived gas $^{81}Kr^{m}$ available from the cyclotron produced ^{81}Rb generator enables detailed study of regional ventilation to be performed by a simple rapid technique at low radiation dose. Such sets of images of regional ventilation and perfusion are performed in various pulmonary diseases and have been compared with chest radiographs.

With pulmonary embolic disease, defects of perfusion with normal ventilation is a pattern frequently associated with a normal chest radiograph. Changes in the vascular pattern can be detected in only a small proportion of such patients.

Pneumonia, collapse and bronchial obstruction without pulmonary collapse are frequently associated with a relative maintenance of regional perfusion and absent ventilation. Parenchymal lung lesions such as those due to emphysema and bullae show matched defects of ventilation and perfusion. A combination of these patterns may occur with multiple pathology. Pneumonia, infarction and pulmonary embolic disease without infarction can all co-exist in the same lung and detailed comparison of the chest radiograph and scan is necessary to elucidate these pathological patterns.

COMPUTED TOMOGRAPHY OF THE THORAX

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Because of the greater sensitivity of computed tomography compared with conventional radiography, more detail shows on pulmonary examinations in normal and abnormal cases.

Gravity perfusion and hypostatic changes become visible, pulmonary vessels in their natural unenhanced state show very densely, and on one section, by using different window settings, all tissues can be seen, including bone and soft tissues as well as lung.

CT is the method of choice in demonstrating metastases, especially if thoracotomy is being contemplated for the removal of a single lesion. In asbestosis, pleural plaques and interstitial disease are shown at an earlier stage or more markedly than on conventional radiography, and CT is invaluable in the demonstration of mediastinal lesions, especially lumph nodes and thymic tumours.

Axial sections are particularly appropriate for radiotherapy planning and for monitoring chemotherapy.

IS ARTERIOGRAPHY OUT OF DATE?

By I. H. Kerr

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In making the choice of investigation for a diagnostic problem one must consider which method is the most effective, reliable, and definitive, the least unpleasant and dangerous, the quickest and the cheapest. The choice will be influenced by the importance of making the full diagnosis, of demonstrating the anatomy of the lesion and also by the urgency. Arteriography has hazards not shared by radio-active isotope studies or computerized tomography. Yet by aortography and pulmonary arteriography diagnostic information of importance can be obtained which cannot be provided by the newer techniques.

Aortography is indicated in patients with anatomical anomalies, aneurysms, dissections, traumatic rupture, coarctation and abnormal connections.

Pulmonary arteriography should be performed in some cases of pulmonary embolism particularly if embolectomy is being considered, in arteriovenous fistulae, in some patients with pulmonary hypertension, in anomalous venous drainage, pulmonary varices and pulmonary artery stenosis. Arteriography is not out of date in the investigation of the lungs and mediastinum.

LUNG IMAGING WITH RADIOACTIVE AEROSOLS

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An assessment of regional ventilation can be useful for (a) improving the accuracy of the lung perfusion scan in the diagnosis of pulmonary embolism; (b) the early diagnosis and functional evaluation of chest diseases, particularly airways obstruction; (c) the differential diagnosis of emphysema and bronchitis.

Continuous inhalation of $^{81}Kr^{m}$ should be considered the technique of choice for ventilation scanning (Fazio *et al.*, 1978). Unfortunately, the availability of $^{81}Rb \rightarrow {}^{81}Kr^{m}$ generators is limited by their relatively short half-life (4.6 hours). Lung images can be obtained, in multiple views, following inhalation of radioactive aerosols. However, in patients with chronic airways obstruction, these images can show very peculiar patterns, which are still largely unexplained. Variability in deposition can also arise from differences in particle size, it being generally accepted that smaller particles penetrate deeper into the bronchial tree. In an attempt to control the diameter of the particles, the use of human albumin minimicropheres labelled with $^{99}Tc^{m}$ ($^{99}Tc^{m}$–HAMM) has been suggested. These particles can be delivered with a modified Venturi nebulizer, the mean diameter of the wet particles at the outflow of the nebulizer being 0.8 μ (range 0.2–2.5 μ). Despite the rather small mean diameter, the images obtained with ^{99}Tc^{m}–HAMM should be, on theoretical grounds, mainly representative of deposition of the larger (2–2.5 μ) particles contained in the preparation. This is because most of the activity will be contained in these large particles, being proportional to particle surface area rather than diameter. In a co-operative study with colleagues at the Royal Free Hospital, the deposition of ^{99}Tc^{m}–HAMM was compared in two normals and in six patients with chronic airflow obstruction, with that of a strictly monodispersed (2 $\mu \pm 0.3$ μ) aerosol. The latter is made of polystyrene particles produced by a spinning disc generator and labelled with ^{99}Tc^{m} (^{99}Tc^{m}–POLY). The two procedures were performed with an interval of 24 hours. ^{81}Kr^{m} ventilation scans and pulmonary functions test were performed on both occasions and confirmed the stability of the respiratory conditions.

In the normal subjects the images obtained with ^{99}Tc^{m}–HAMM, ^{99}Tc^{m}–POLY, and ^{81}Kr^{m} were almost identical, showing a uniform distribution of activity to the lung periphery. In the patient group the images obtained with ^{99}Tc^{m}–HAMM and ^{99}Tc^{m}–POLY showed a very inhomogeneous distribution of activity which was concentrated in "hot" spots scattered throughout the lungs, probably due to areas of bronchial deposition. Despite the very bizarre distribution, the images obtained with ^{99}Tc^{m}–HAMM and ^{99}Tc^{m}POLY were almost identical, as confirmed by a quantitative computer comparison. In these patients, the ^{81}Kr^{m} ventilation scan had a more homogenous, non-spotty appearance.

These data indicate that (a) radioactive aerosol techniques are reproducible in normals or patients. (b) the ^{99}Tc^{m}–HAMM images are mainly representative of deposition of the larger (2.0–2.5 μ) particles, reflecting the fact that these contained most of the activity. The critical factor seems, therefore, to be the maximum diameter of the particles, rather than the mean diameter. This should be kept in mind when developing techniques for aerosol imaging. (c) Aerosol techniques yield, in the absence of airways obstruction, images which are fairly representative of regional ventilation. They can, therefore, be considered as a complement to lung perfusion scans for the diagnosis of pulmonary embolism. (d) The bronchial deposition observed in patients with airways obstruction can be used for the early detection of chest diasese. It is conceivable that this deposition would be reduced by using mono- or polydispersed aerosols with a maximum diameter not exceeding 1.0 μ

REFERENCE

FAZIO, F., LAVENDER, J. P., and STEINER, R. E., 1978. ^{81}Kr^{m} ventilation and ^{99}Tc^{m} perfusion scans in chest disease: comparison with standard radiographs. *American Journal of Roentgenology*, *130*: 421–428.

Appeal for certain back issues

If you have copies of any January, February, March and June, 1977 issues of this journal (BJR, Vol. 50, 589, 590, 591, 594) which you do not require could you please return them to The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG, England, for redistribution to subscribers who are unable to obtain copies.

The Institute will refund second class postage, plus any prepayments you have made for the issues you return (only applies to January, February, March and June, 1977 numbers).

Forthcoming events

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).

Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

RADIOBIOLOGY MEETINGS

The following meetings are scheduled at the Institute: "Radiation chemists talk to biologists", January 19, 1979. It is expected that the majority of papers will convey the implications or applications of radiochemical and related studies in biology or medicine, *e.g.* sensitizers, phototherapy.

"Preview of papers for the International Congress, Japan" April 20, 1979. This will be a general meeting, and proffered papers are invited from people preparing to go, even if finally not funded. Titles and brief preliminary abstracts should reach Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, by March 15, 1979.

Further information can be obtained from the General Secretary, The British Institute of Radiology (01–935 6237).

PROBLEMS OF BENIGN AND MALIGNANT BONE TUMOURS

A joint evening meeting organized by the Royal Society of Medicine (Section of Radiology), The British Institute of Radiology and the Royal College of Radiologists, to be held on Friday, January 19, 1979, at the Royal Society of Medicine, London.

Speakers: Dr. Mary Catto, Dr. P. Jacobs, Mr. D. R. Sweetnam and Dr. G. E. Flatman.

Further information: contact the Royal Society of Medicine.

CLINICAL ONCOLOGY SYMPOSIUM ON THYROID CANCER

The Royal College of Radiologists will be holding a multi-disciplinary symposium on January 26–27, 1979. It will be held at 66 Portland Place, London W1N 4AD and is intended for senior registrars, consultants and research workers. Selected topics on the subject of thyroid cancer will be reviewed by authoritive speakers from the United Kingdom. The registration fee is £25.

Full details of the symposium can be obtained from the Meetings Secretary, Royal College of Radiologists, 28 Portland Place, London W1N 4DE.

NEW RADIOPHARMACEUTICALS INCLUDING ^{123}I

An all day meeting organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on Wednesday, February 14, 1979 at the Middlesex Hospital Medical School.

Further information and registration from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

IMAGING IN NUCLEAR MEDICINE

An evening meeting to be held on Thursday, February 15, 1979 at The British Institute of Radiology, 32 Welbeck Street, London, W1, organized jointly by The British Institute of Radiology, the Royal College of Radiologists and the Royal Society of Medicine (Section of Radiology).

Further information contact the General Secretary, The British Institute of Radiology.

WORKSHOP ON THE USE OF COMPUTERIZED TOMOGRAPHIC SCANNERS IN RADIOTHERAPY

Following the successful workshop meeting on "The Use of Computers in Radiotherapy in Europe", held at the International Atomic Energy Agency in July 1976, the Commission Informatique of the European Association of Radiology will hold a workshop on the "Use of Computerized Tomographic Scanners in Radiotherapy", at the headquarters of the World Health Organization on March 28–30, 1979.

The meeting is designed to promote discussions among therapeutic and diagnostic radiologists, physicists and computer experts with previous experience in this field and will be limited strictly to 150 participants.

The programme will include invited and proffered papers and discussions concerning the recognition and definition of tumour and target volumes and treatment planning as well as future directions for development. The proceedings will be published.

Further information can be obtained from the General Secretary, Professor R. J. Berry, Department of Oncology, The Middlesex Hospital Medical School, London W1P 7PN.

1979 THE BRITISH INSTITUTE OF RADIOLOGY ANNUAL CONGRESS

The 37th British Institute of Radiology Annual Congress and Scientific Exhibition will be held at the Middlesex Hospital Medical School on April 26–27, 1979. Included in a programme of invited papers on diagnosis, therapy, radiological physics and nuclear medicine topics will be the Presidential Address by Mr. W. M. Ross entitled *The Institute, yesterday and tomorrow*, and the Silvanus Thompson Memorial Lecture by Professor G. E. Adams on *Past, present and future of hypoxic cell sensitizers.*

Details and registration from The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

MACKENZIE DAVIDSON MEMORIAL LECTURE

To be given by Dr. G. B. Schofield, Medical Officer, British Nuclear Fuels Ltd., on *Biological control in a plutonium production facility* at The British Institute of Radiology, 32 Welbeck Street, London, W1 on Thursday, May 17, 1979.

INTERNATIONAL SYMPOSIUM ON PERCUTANEOUS BIOPSY AND THERAPEUTIC VASCULAR OCCLUSION

To be held May 7–9, 1979 in Munich. Topics of biopsy: bone, lung, mediastinum, pancreas, kidney, liver, lymph-nodes, mammary gland. Topics of vascular occlusion: G.I. tract, lung, liver, kidney, cervicofacial, cerebromedullary, gynecologic, traumatic and pathologic bleeding.

Application and information: Prof. Dr. H. Anacker, Institut für Röntgendiagnostik der Technischen Universität, Klinikum r.d.I., Ismaningerstr. 22, D-8000 München 80.

INTERNATIONAL SYMPOSIUM ON INTERVENTIONAL RADIOLOGY

An E.A.R. Symposium, organized by the Portuguese Society of Radiology and Nuclear Medicine, will be held May 30–June 2, 1979 in the Algarve, Portugal.

Proposed sessions include vascular therapy; selective embolization and management; catheter implantation in chemotherapy and percutaneous treatments; ultrasonic guiding techniques and nuclear imaging as a guiding technique for biopsy and fluid aspiration.

For further information contact the Portuguese Society of Radiology and Nuclear Medicine, 123, 1.° Esq., Avenida Elias Garcia, Lisbon 1, Portugal.

NON-INVASIVE IMAGING IN MEDICINE: HEART, LIVER, PANCREAS

A symposium arranged by the medical faculty of the University of Lund, Sweden, on June 6–9, 1979, with participation of prominent speakers in the field of CT-scanning, ultrasonography, and nuclear scanning.

For further details and registration, contact Miss Karin Jönsson (secretary), Department of Diagnostic Radiology, University Hospital, S-221 85 Lund, Sweden.

INTERNATIONAL COURSE IN CHEST RADIOLOGY

International Course in Chest Radiology and other aspects of chest disease, Stockholm, Sweden, June 11–13, 1979.

Organized by the *Fleischner Society*, a non-profit organization in memory of Felix Fleischner, Harvard University, Boston.

Information and application forms from: Björn Nordenström, M.D., Professor of Radiology, c/o Reso Congress Service, S-105 24 Stockholm, Sweden.

NUCLEAR CARDIOLOGY

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on June 20, 1979 at the Institute House.

Further information contact the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

4TH CONGRESS OF THE EUROPEAN ASSOCIATION OF RADIOLOGY

Will be held in Hamburg, W. Germany, on September 2–9, 1979.

QUANTITATION OF TUMOUR RESPONSE: A CRITICAL APPRAISAL

The L. H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to simulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.
Factors of prognostic significance.
In vitro assays of tumours excised after treatment *in vivo*.
The choice of suitable experimental models in rodents.
The role of human tumour xenografts.
Statistical evaluation of tumour response data.
The limitations and artefacts of each assay technique.
The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

RECENT ADVANCES IN BRAIN SCAN

Bordeaux, September 20–22, 1979. Under patronage of Université de Bordeaux II and Institut National de la Santé et de la Recherché Médicale (INSERM), Professor J. M. Caille and G. Salamon are organizing in Bordeaux a meeting devoted to "Recent Advances in Brain Computed Tomography".

Subjects: Physical basis of computed tomography by transmission: normal and pathologic results and their correlation. Other methods of tomography (neutron scanner, emission scanner, etc.).

The languages used will be French and English. Fees: F.F.500.

For any information: Professor Caille, Service de Neutroradiologie, Hôpital Pellegrin-Tripode, 33076 Bordeaux. Tel. (56) 96 83 83, poste 4603.

Membership Subscription Reminder

Members of the British Institute of Radiology are reminded that new membership subscription rates become effective on January 1, 1979, as follows:

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UNITS, SYMBOLS AND ABBREVIATIONS

Authors are encouraged to adopt the *International System of Units (SI)* (B.S.I., 1970; W.H.O., 1975). The publication *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (Royal Society of Medicine, 1977) is thoughtful and critical on this subject; authors are strongly recommended to follow the detailed suggestions in this guide and to note particularly the comments made on the choice of units. From Volume 53 (starting January 1980) units of radiation should be given in SI with the old units in parenthesis, thus 1 Sv (100 rem), 200 cGy (rad), 1 MBq (27 μCi). Some explanation and a table of conversions appeared in an Editorial, Vol. 52, page 1, 1979.

DIAGRAMS AND GRAPHS. Diagrams and graphs, including numerals and lettering, should be clearly drawn in black ink for photographic reproduction to a width of 76 mm (exceptionally 156 mm). Good quality photographic prints or the original art work should be supplied. Care should be taken that details such as numbering and experimental points remain legible after photographic reduction. Computer print-outs are seldom satisfactory. The figure number, author's name and title of article should be pencilled lightly on the back of each illustration.

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Examples

Brownell, G. L., Aronow, S., and Hine, G. J., 1967. Radioisotope scanning. In *Instrumentation in Nuclear Medicine*, Ed. G. J. Hine, Vol. 1, pp. 381–428 (Academic Press, New York).

Watson, A., Russell, J. G. B., and Torrance, G. B., 1970. Hepatic blood flow and Biligrafin excretion during intravenous cholangiography. *British Journal of Radiology*, *43*, 248–250.

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SUPPLEMENTS AND REPORTS. Examples of material considered for publication as Supplements or in the Report Series are special monographs which are too long for publication within the Journal, or detailed reports of certain meetings.

REFERENCES

British Standard 3763, 1970. *The International System of Units (SI)*, British Standards Institution, London (£2·70).

Institute of Physics, 47 Belgrave Square, London, S.W.1, 1976. *Notes for Authors.*

The Royal Society of Medicine, 1 Wimpole Street, London, W1M 8AE, 1977. *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (54p).

W.H.O., 1975. *A Guide to International Recommendations on Names and Symbols for Quantities and on Units of Measurement* (Sw.Fr.48).

Book reviews

Emmett's clinical urography. An atlas and textbook of roentgenologic diagnosis 13
Thermo-radio-therapie 50

Books received

Receipt of the following books is acknowledged as a courtesy to the sender. These publications have been lodged in the Library of The British Institute of Radiology for the use of Members.

Biology of brain tumors. (A series of Workshops on the Biology of Human Cancer, Report no. 5). Edited by O. C. Laerum, D. D. Bigner and M. F. Rajewsky. 1978, pp. 209 (International Union Against Cancer, Geneva) Sw. fr. 15. ISBN 92-9081-030-7.

An international neutron dosimetry intercomparison. ICRU Report 27, 1978, pp. viii+54 (International Commission on Radiation Units and Measurements, Washington). ISBN 0-913394-46-7.

YEAR BOOK OF NUCLEAR MEDICINE 1978. Edited by J. L. Quinn, III; Associate Editor, S. M. Spies. pp. 390 (Year Book Medical Publishers, Inc.; Chicago: London), £21·25.

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EDITED BY Professor G. H. duBoulay

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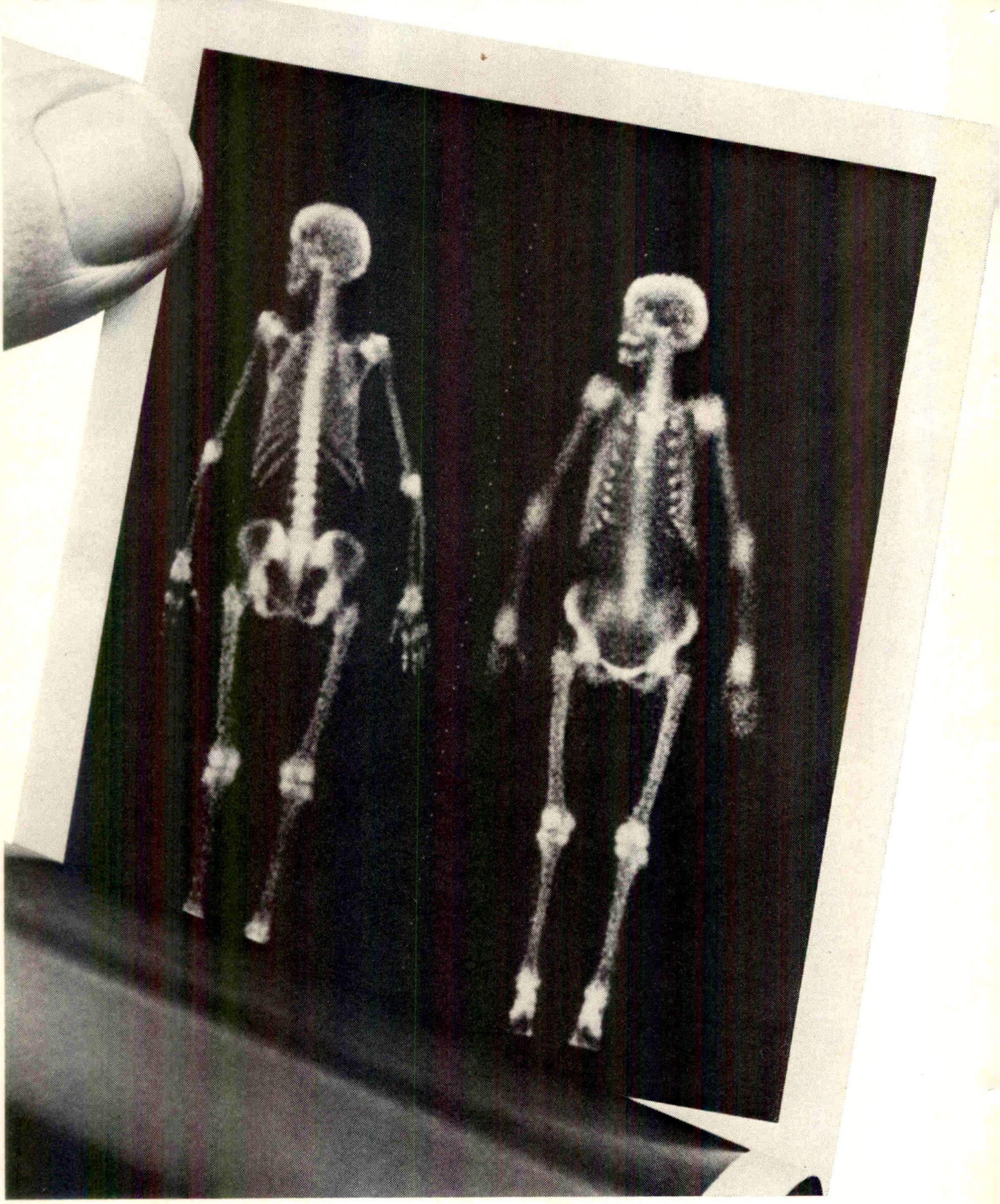

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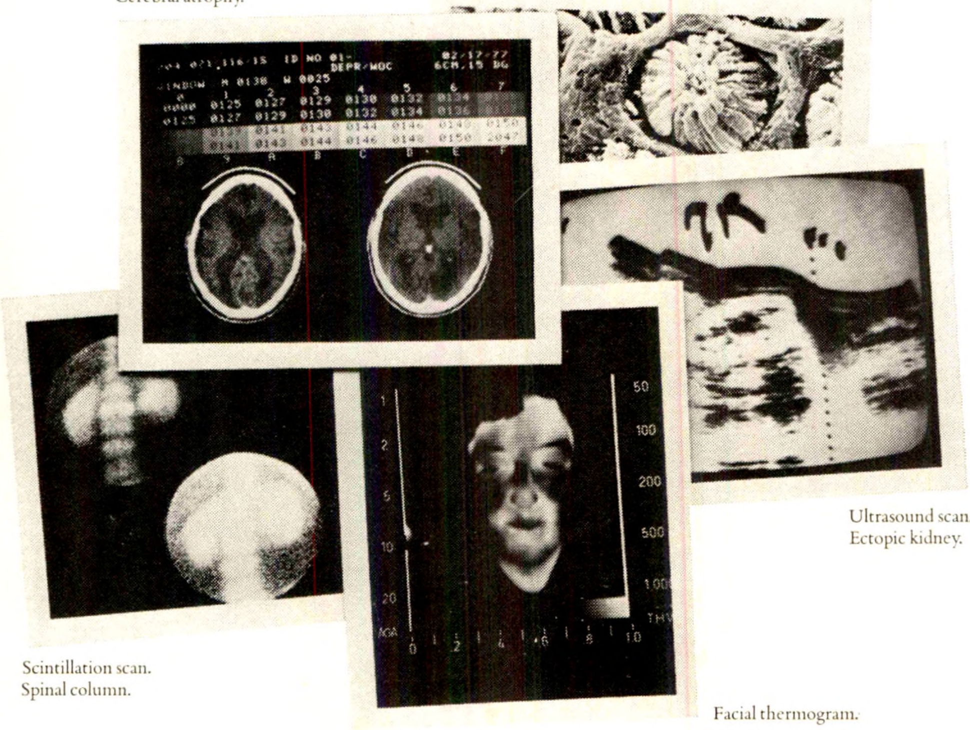

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The hospital is accredited for two out of the three years of training.

Salary: $A24762–33698 per annum (present exchange rate £1=$A1.69).

The right of limited private practice is presently under negotiation.

Initially, employment will be for a period of up to three years although an extension may be negotiated. Four weeks' annual leave and generous sick leave are provided. Fares to Brisbane for the appointee and family may be paid and assistance may be provided for the removal of furniture and effects.

Enquiries should be directed to the Director (Medical Services), Brisbane, telephone 225 2203.

Applications including details of qualifications and experience should be forwarded to the Deputy Commissioner, Department of Veterans' Affairs, Box 651 G.P.O. Brisbane, Queensland 4001.

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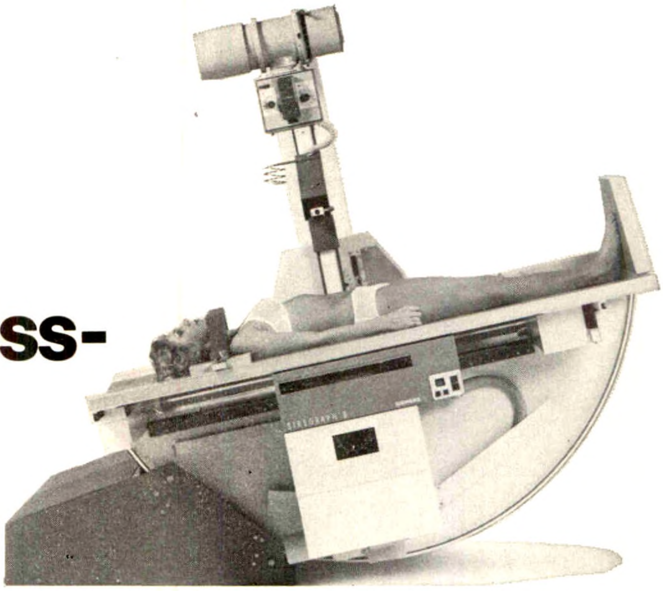

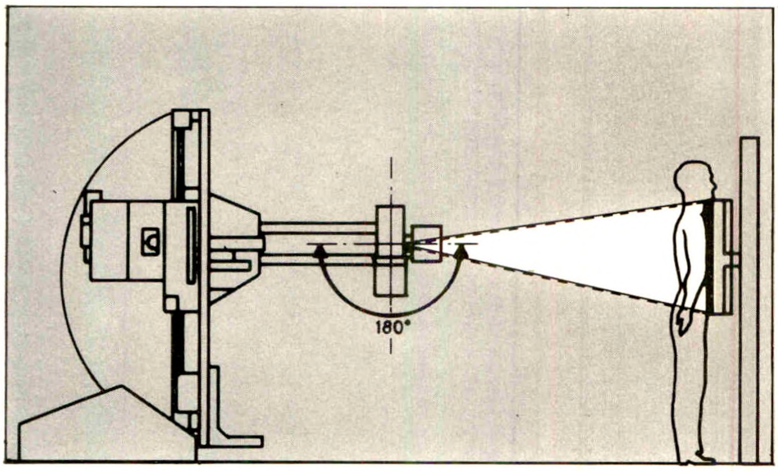

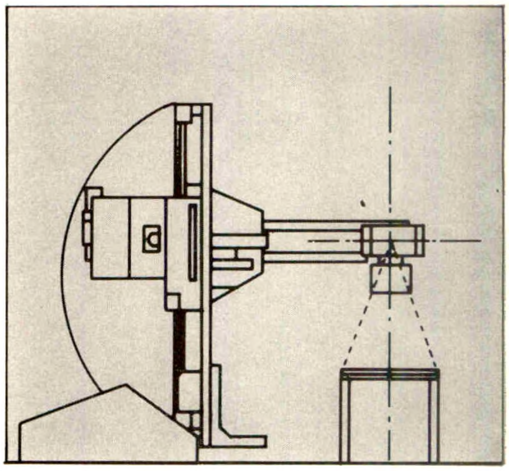

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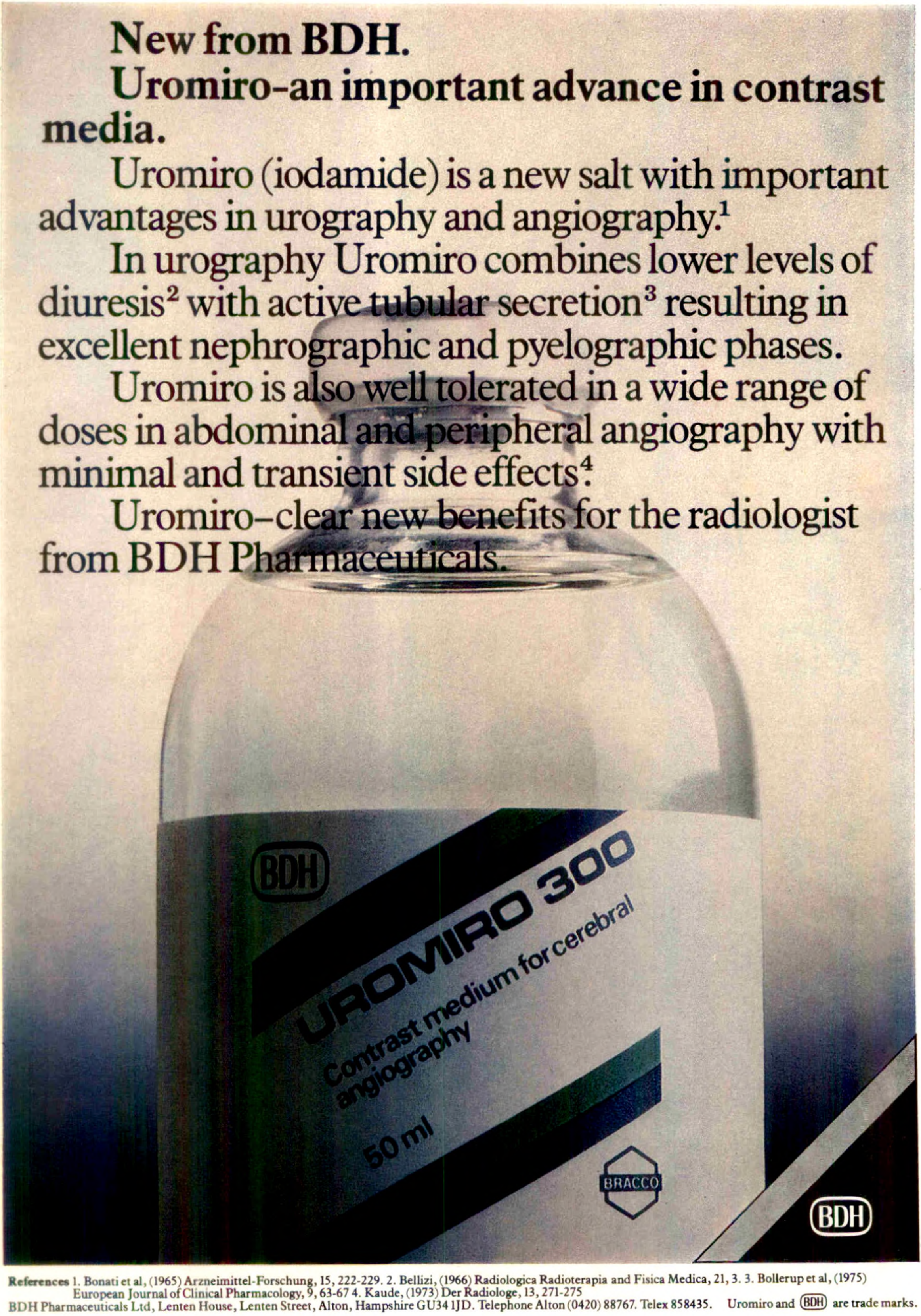

References 1. Bonati et al, (1965) Arzneimittel-Forschung, 15, 222-229. 2. Bellizi, (1966) Radiologica Radioterapia and Fisica Medica, 21, 3. 3. Bollerup et al, (1975) European Journal of Clinical Pharmacology, 9, 63-67 4. Kaude, (1973) Der Radiologe, 13, 271-275
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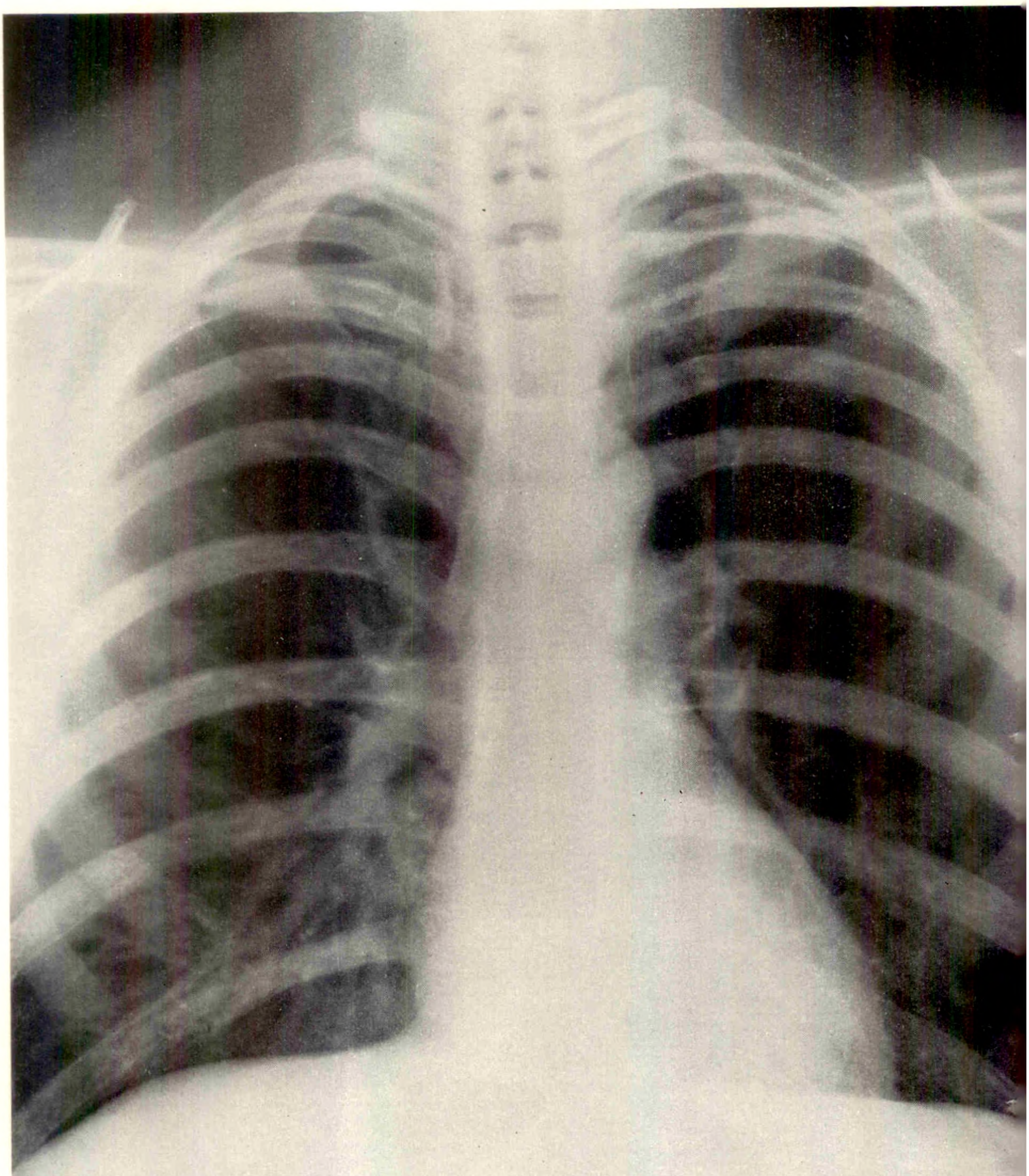

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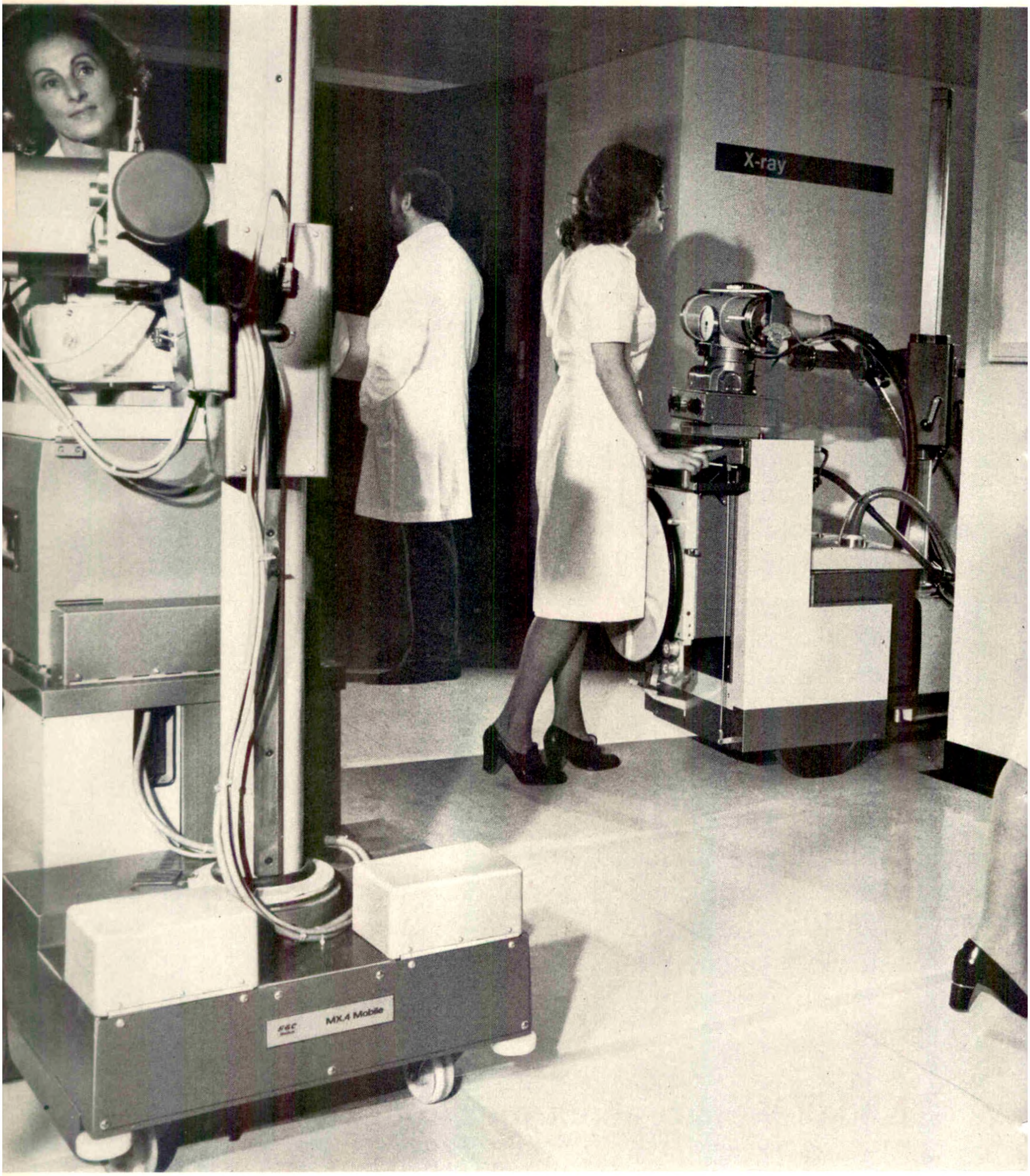

Left: MX4 125 kV, 150 mA. Centre: D38 125 kV, 300 mA. Right: CD38 125 kV, 50 mAS.

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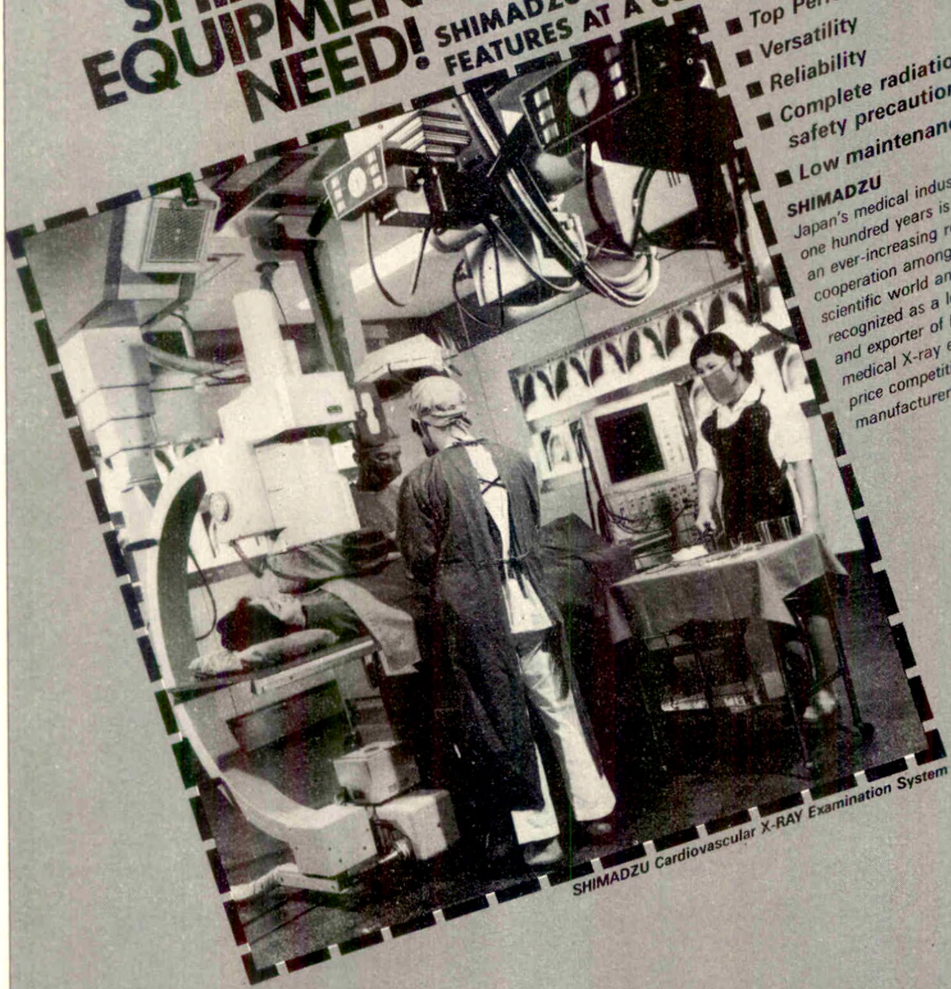

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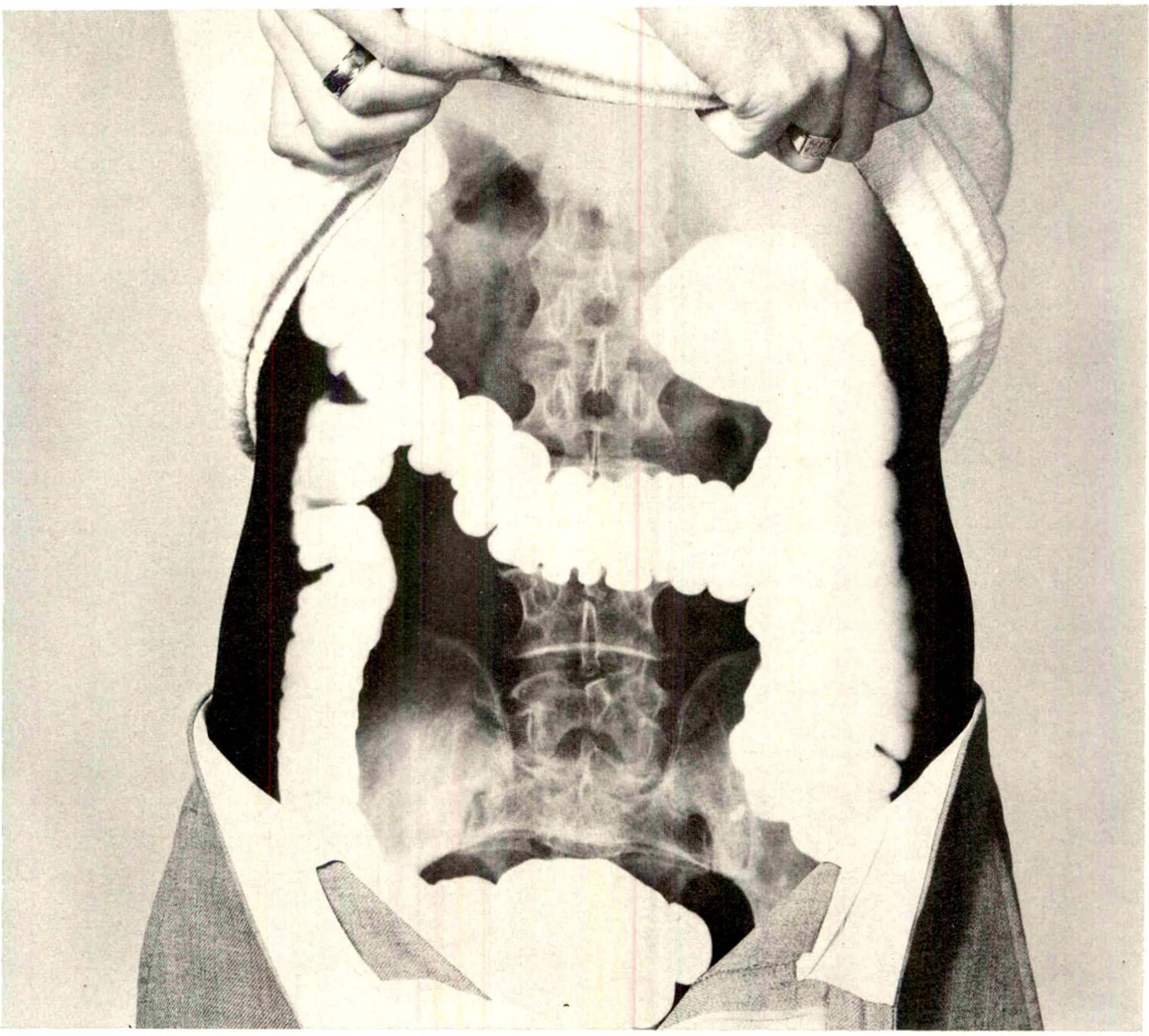

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Director, Department of Radiology

Applications are invited from suitably qualified Medical Practitioners for the post of Whole Time Director, Department of Radiology, which is of Specialist status.

The successful applicant will be responsible for the organisation of Radiological services for the Southland Hospital Board at Southland Hospital, Seddon Memorial Hospital, Gore; and Lake County Hospital, Frankton. The Board area has a catchment population of approximately 120,000.

Southland Hospital is an expanding provincial base hospital with a present bed state of 360 which will increase to 450 when the new Obstetric Unit is opened in March 1979. The Southland Hospital provides a comprehensive range of clinical services and the Department of Radiology is well equipped, having been commissioned in 1970. It includes facilities for Diagnostic Radiology, Ultrasound Scanning and Nuclear Scanning, and a medical staff establishment of four Radiologists and a Registrar with a full complement of Radiographer Technologists and other supporting staff. A School of Radiography is attached to this Department.

Seddon Memorial Hospital (40 miles from Invercargill), has 100 beds and the Radiology Department has been recently upgraded and is well equipped. It is supervised by a well qualified and experienced Charge Radiographer.

Lake County Hospital, 120 miles from Invercargill, is a small country hospital and has a small X-ray Department where the work is carried out by a Staff Radiographer. Plans for a new hospital at Queenstown have been prepared and it is envisaged that when complete, the Radiology services will have been considerably upgraded.

Invercargill is the provincial centre of a wealthy rural and industrial community which has excellent educational and recreational facilities. Within easy reach are lakes and rivers for fishing and boating activities, and in the Winter, full facilities for skiing.

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Application form, conditions of appointment and other information available from Chief Executive Officer, Southland Hospital Board, P.O. Box 39, Invercargill, New Zealand, with whom applications close on March 31, 1979.

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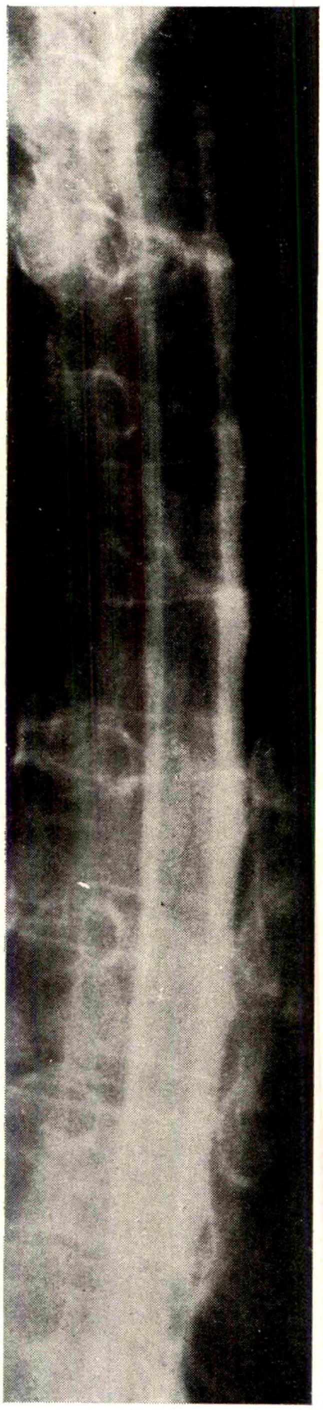
THORACIC MYELOGRAPHY



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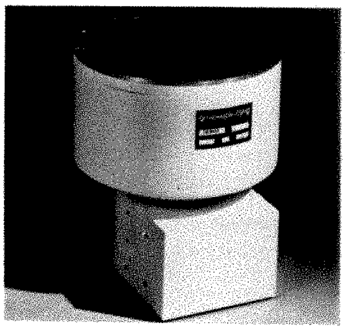

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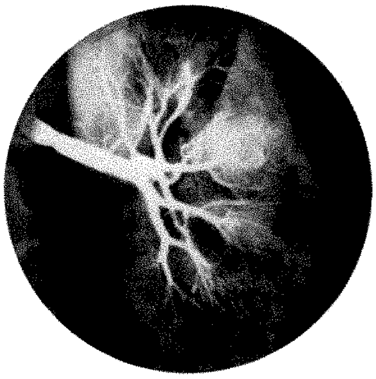
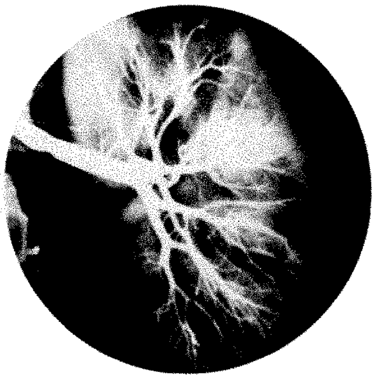


Image obtained with conventional X-ray image intensifier tube



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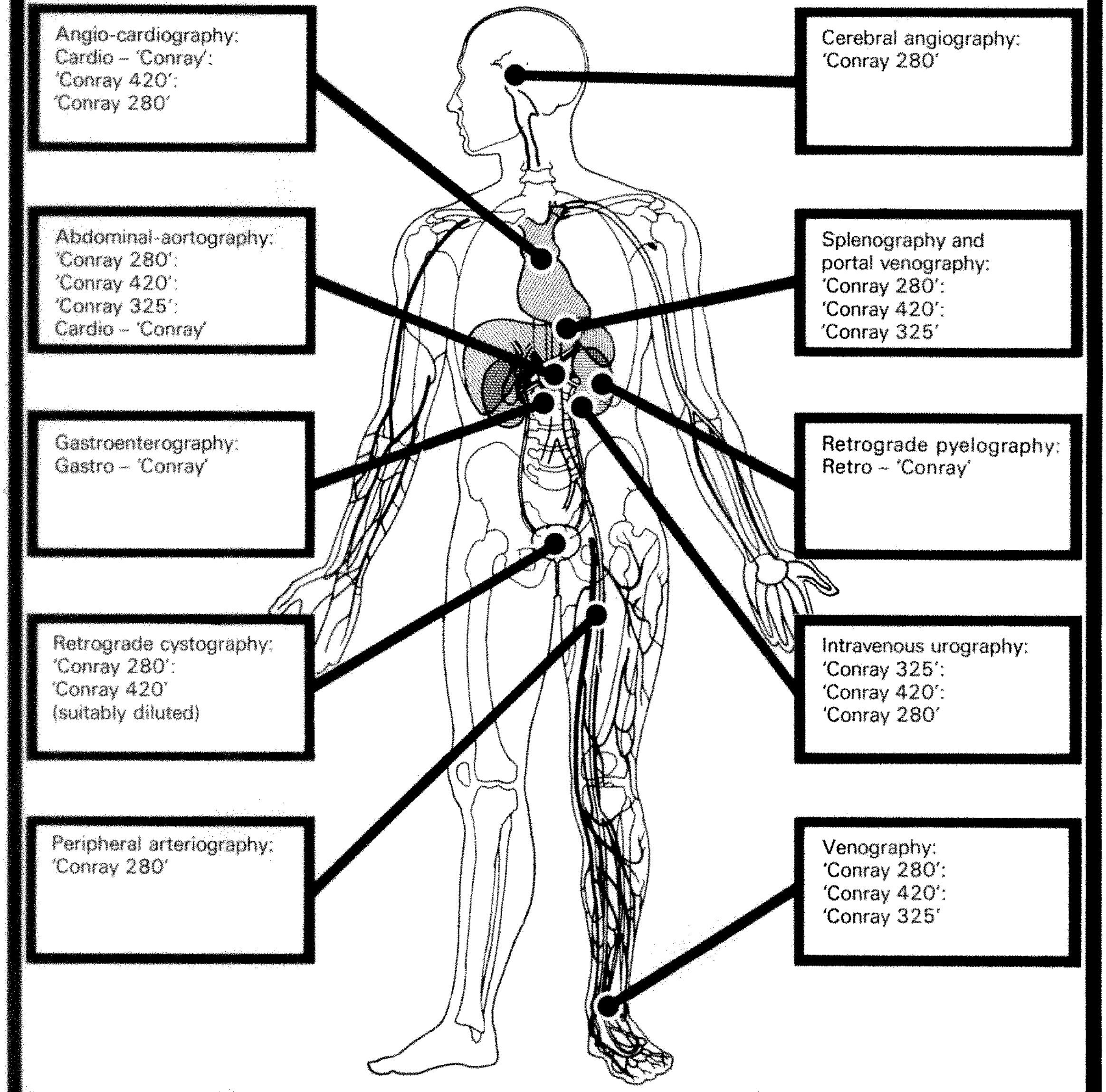

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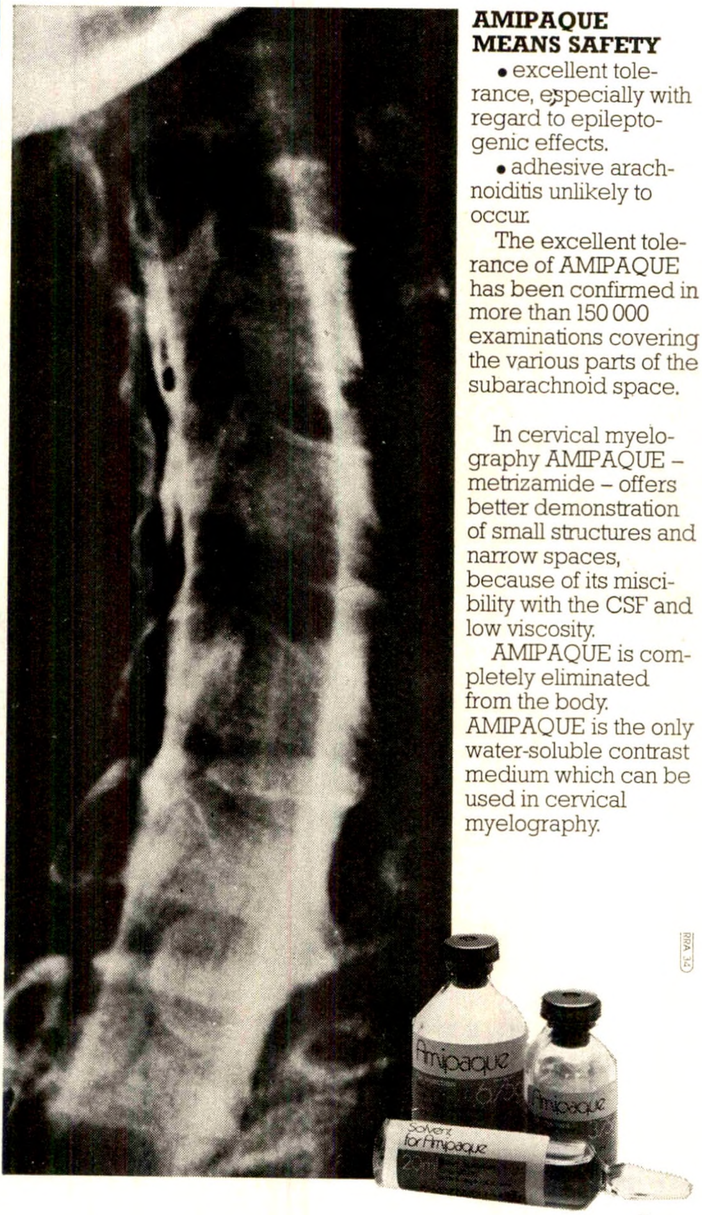
CERVICAL MYELOGRAPHY



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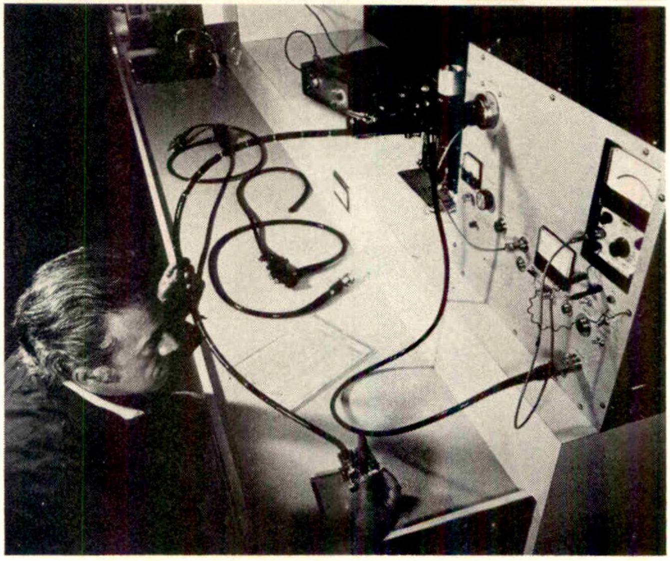

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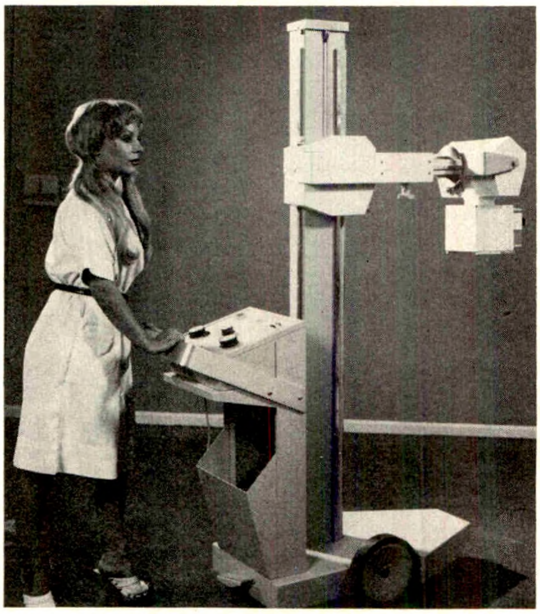

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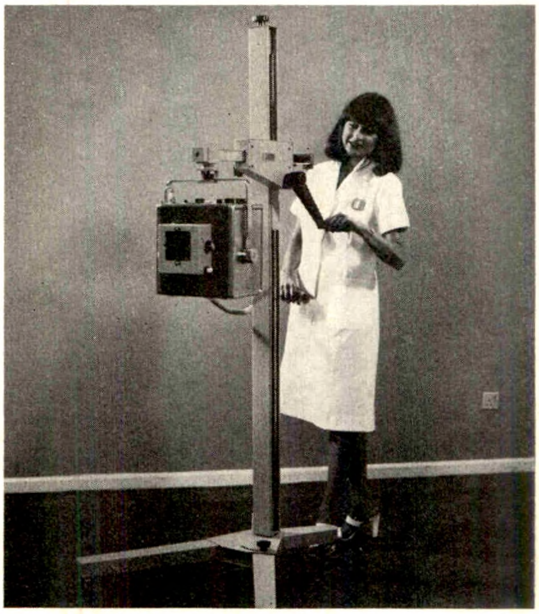

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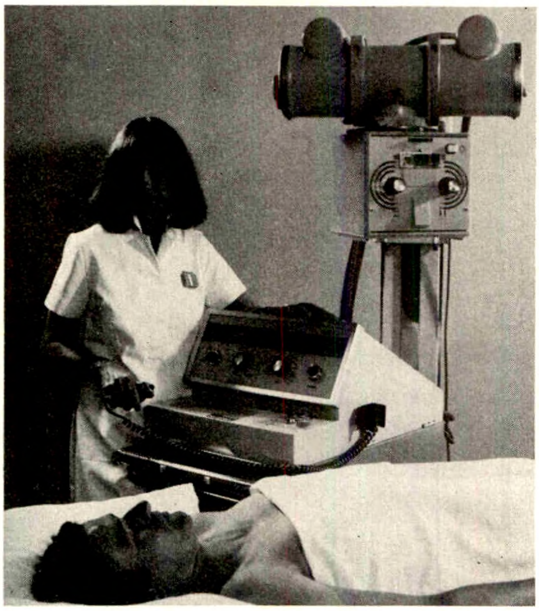

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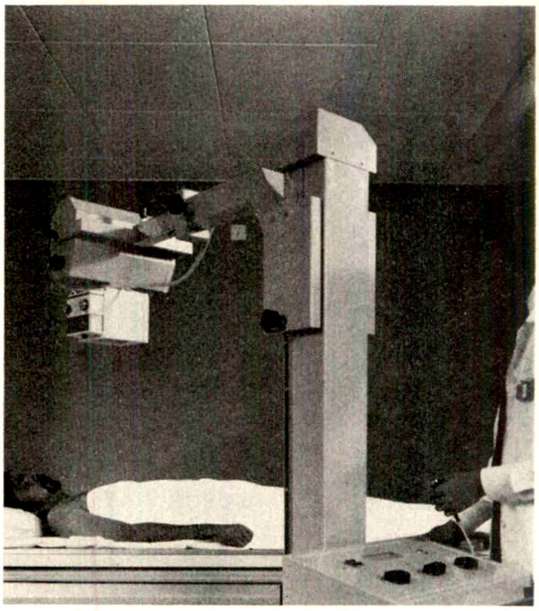

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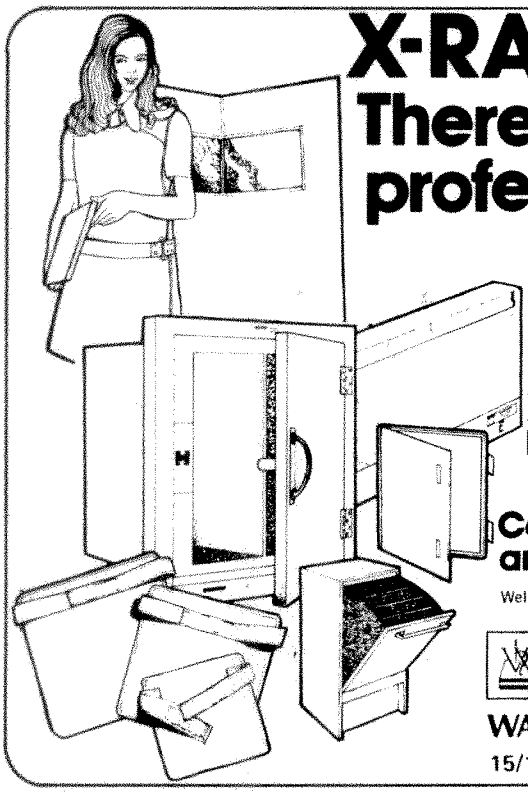

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Entries are invited for the above Prize which is awarded by the Faculty of Medicine and Dentistry of the University for the most outstanding contribution to the advancement of radiology in the year 1978/9 up to the closing date for entries.

The Prize is open to radiologists working in the West Midlands Regional Health Authority, academic staff and the University of Birmingham and graduates of the University working in recognized centres. Criteria for the award include publications, contributions to teaching and/or research and active participation in national or international gatherings related to radiology.

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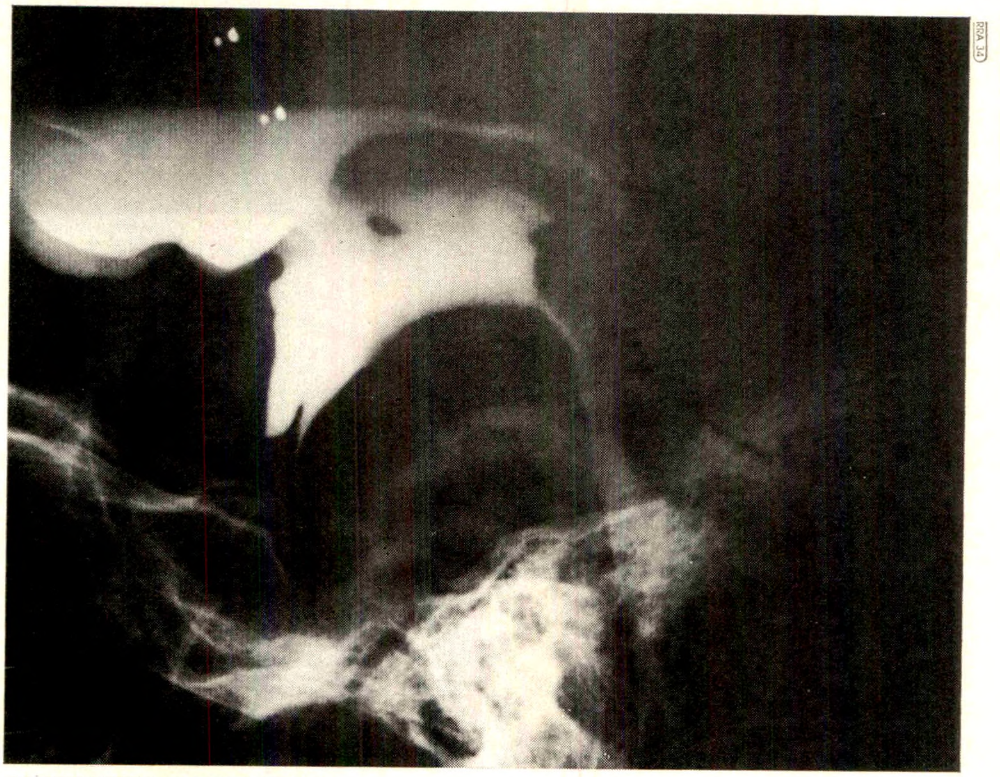

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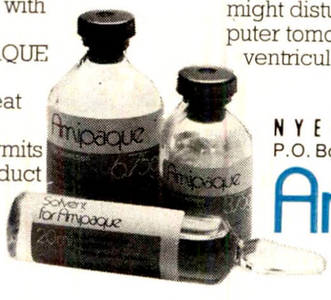

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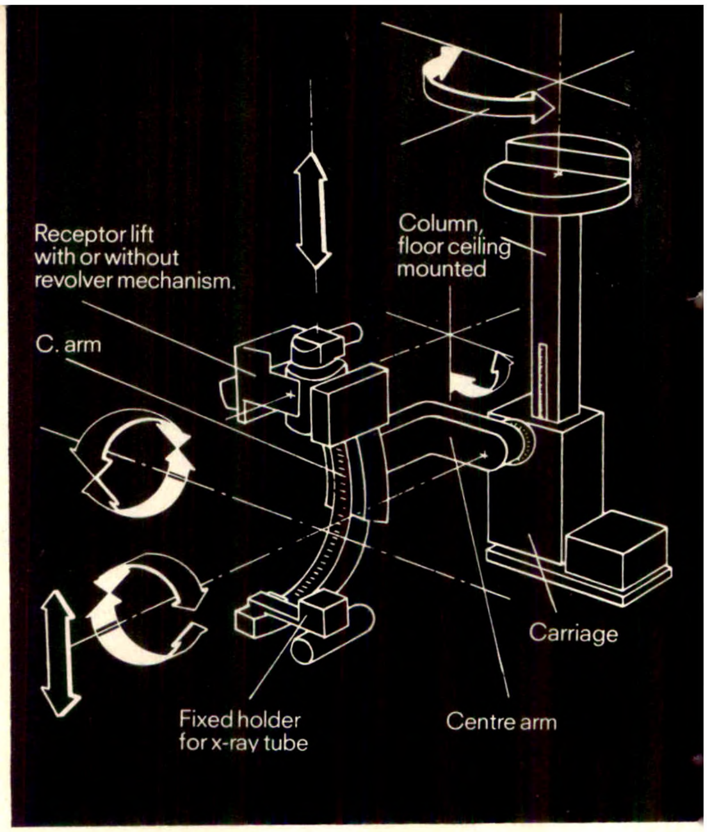
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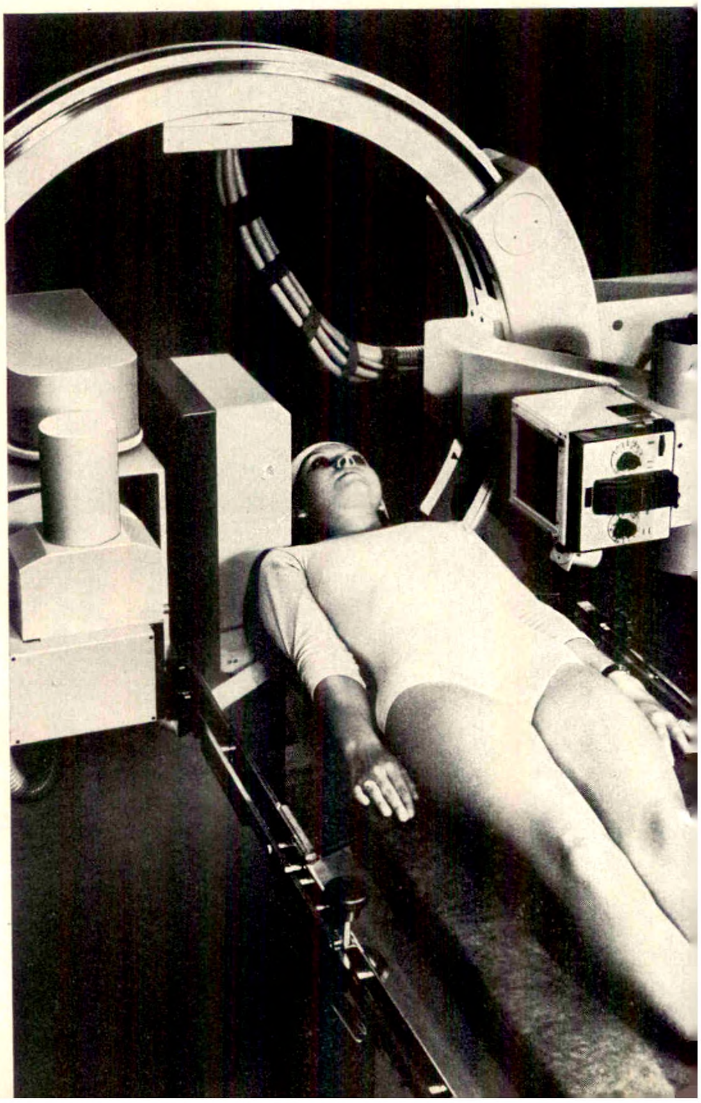

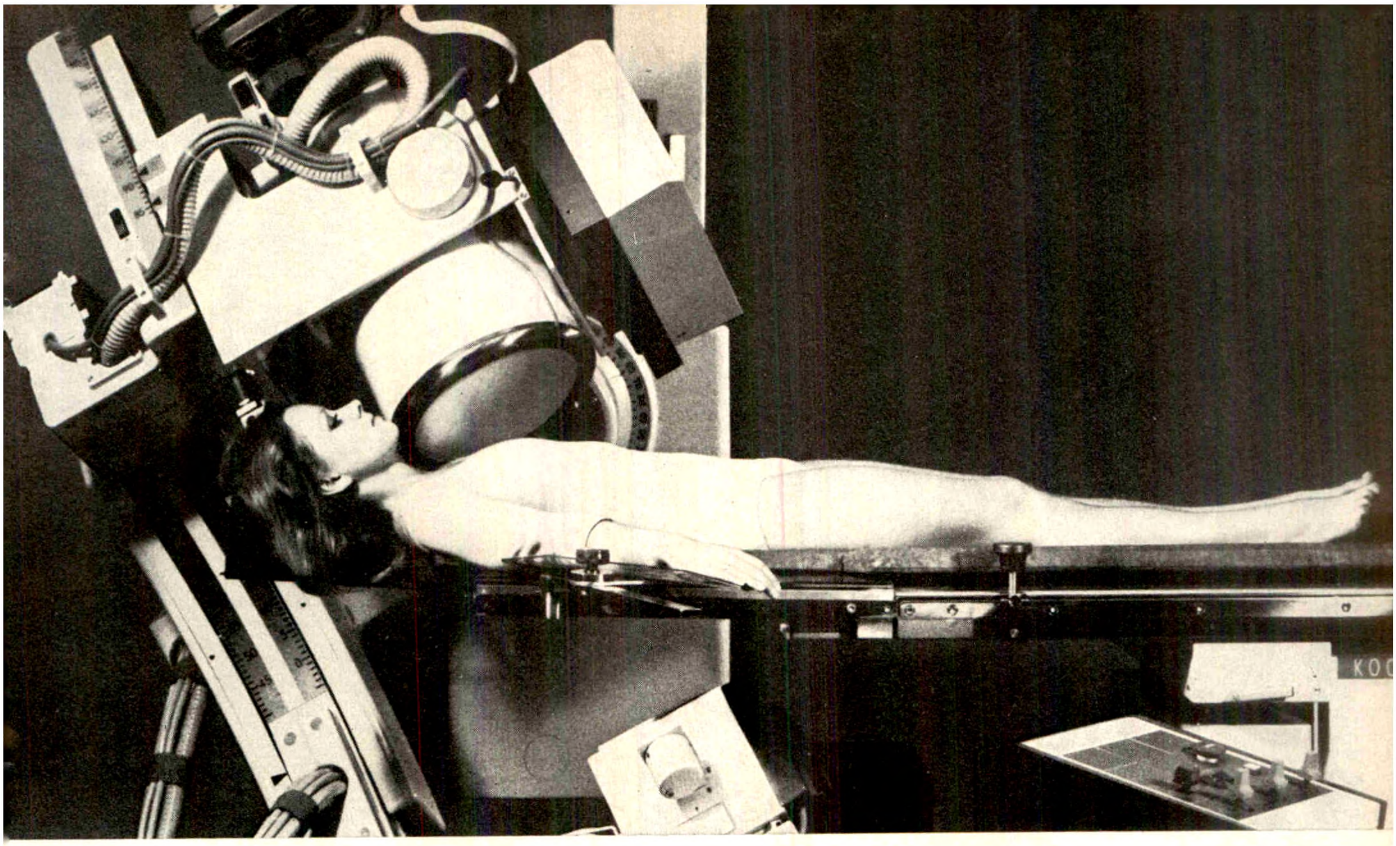
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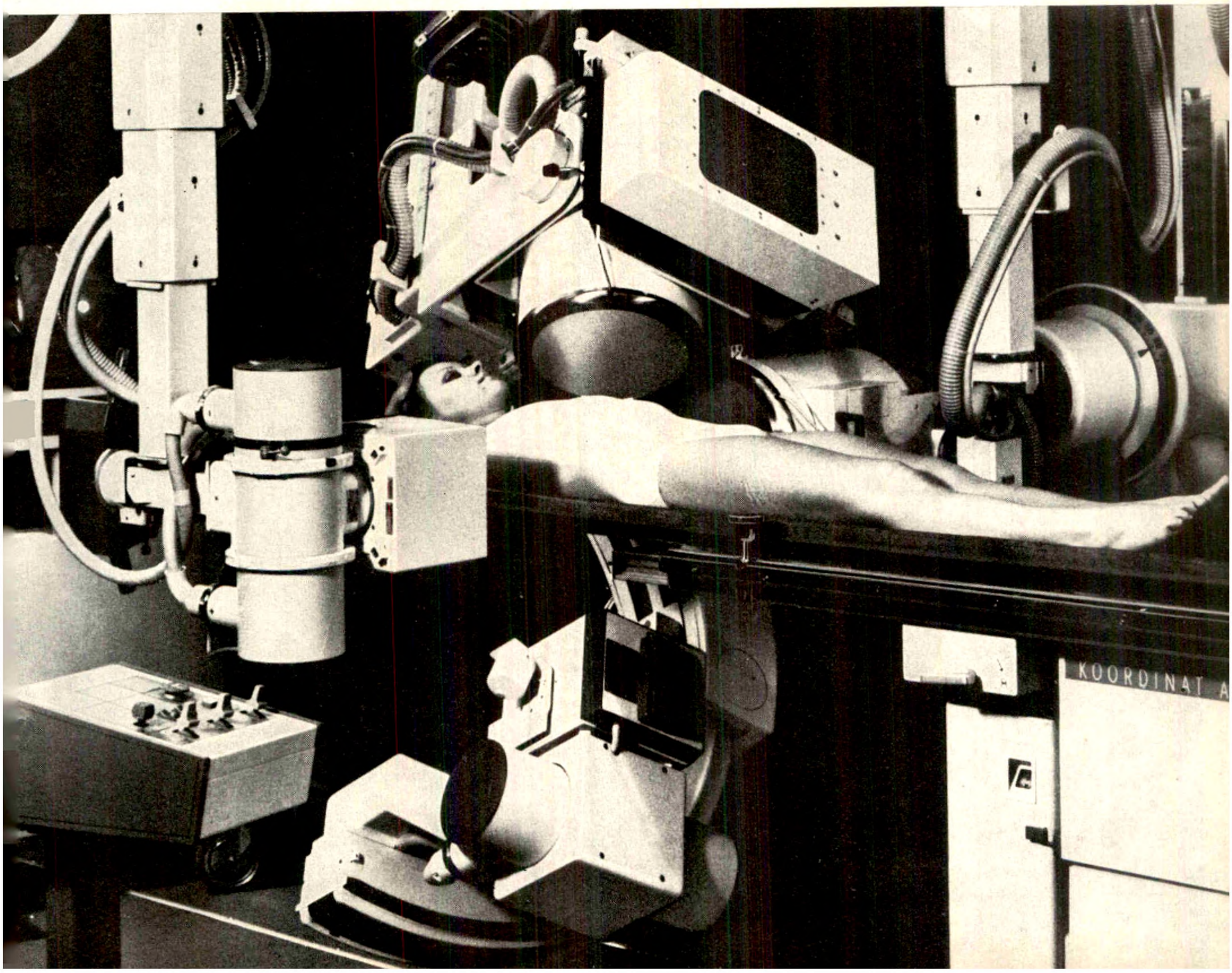
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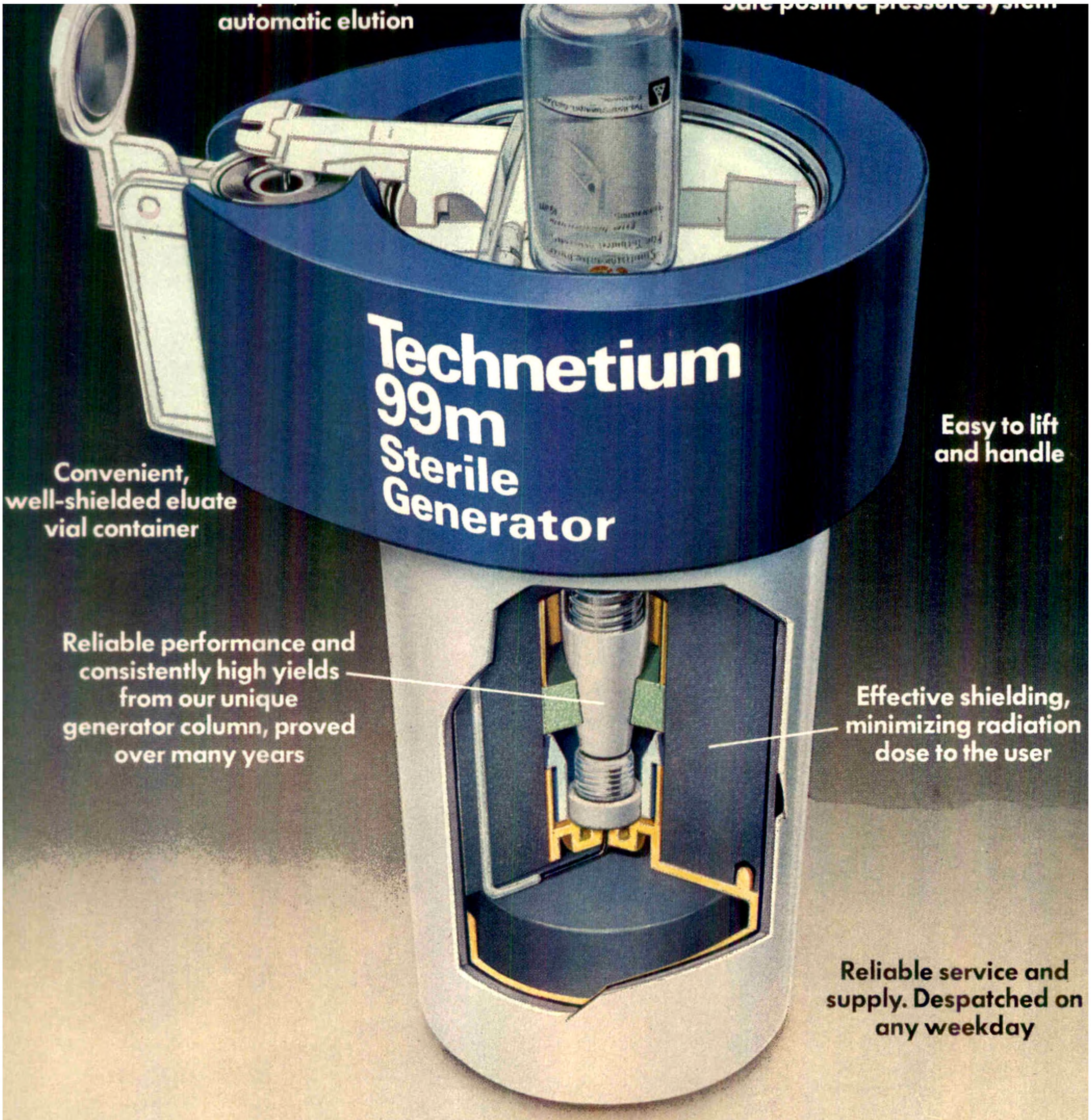
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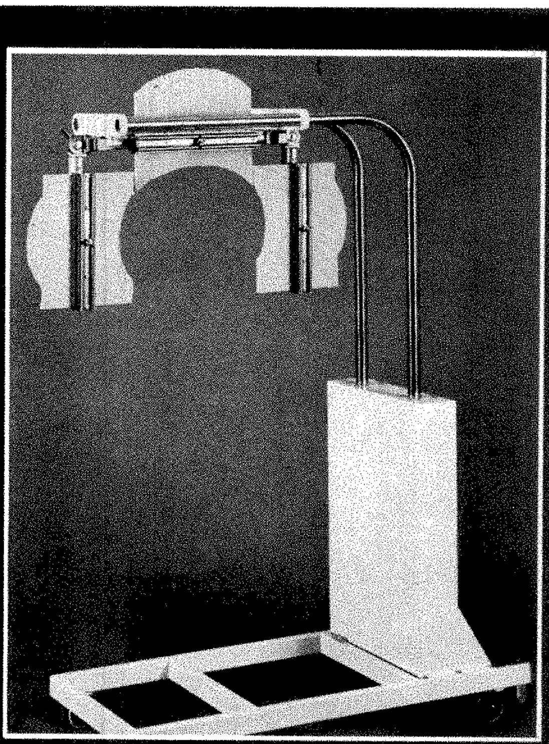

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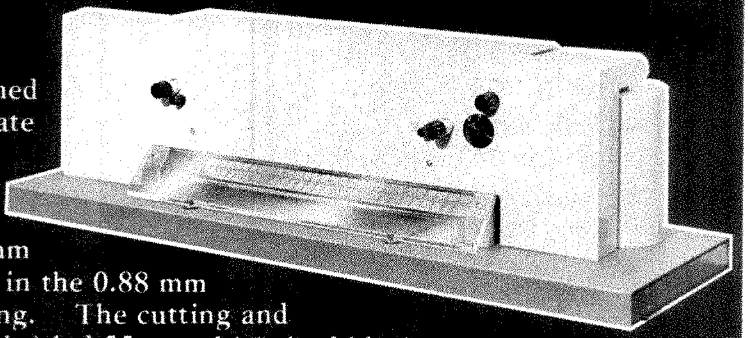

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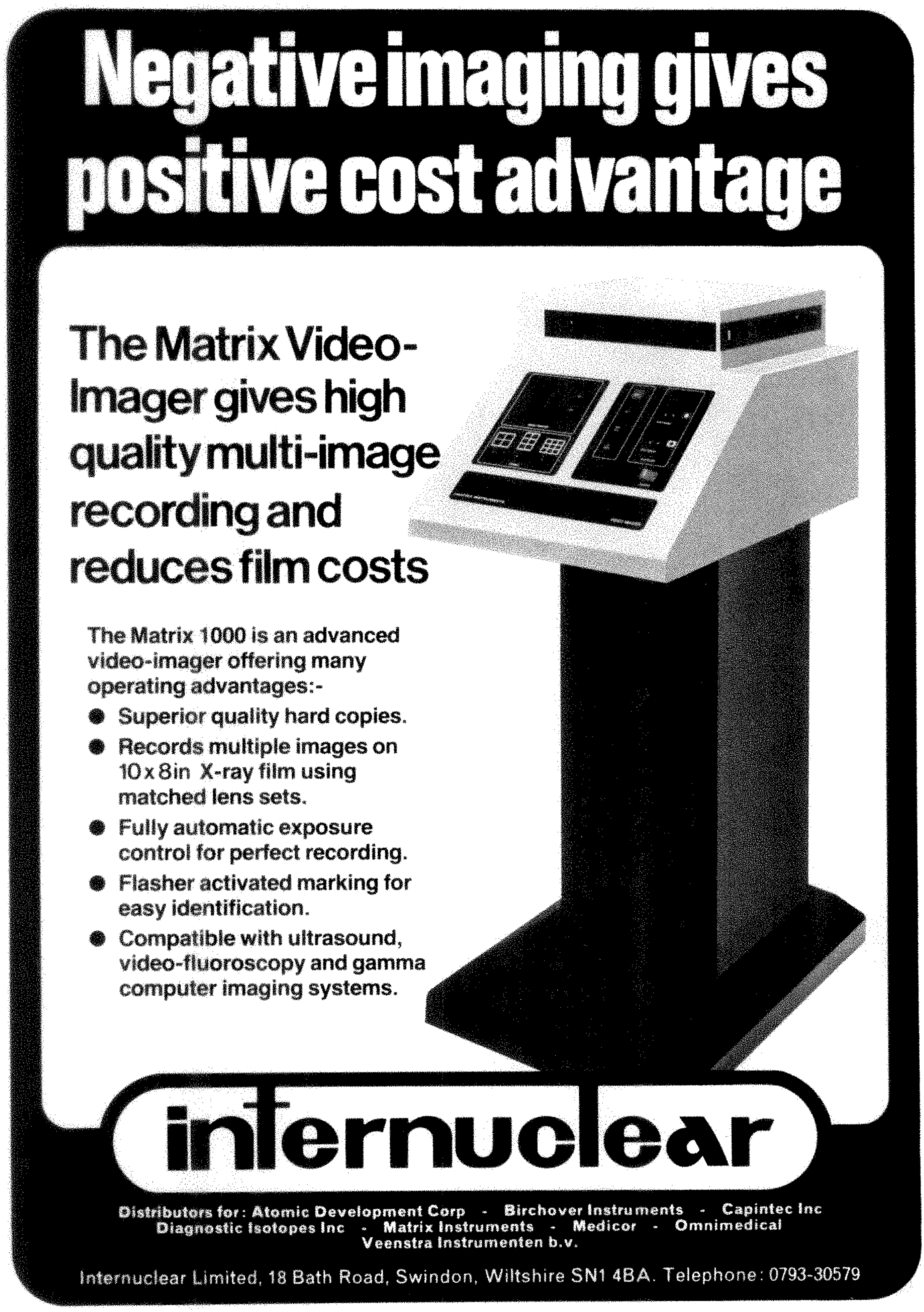

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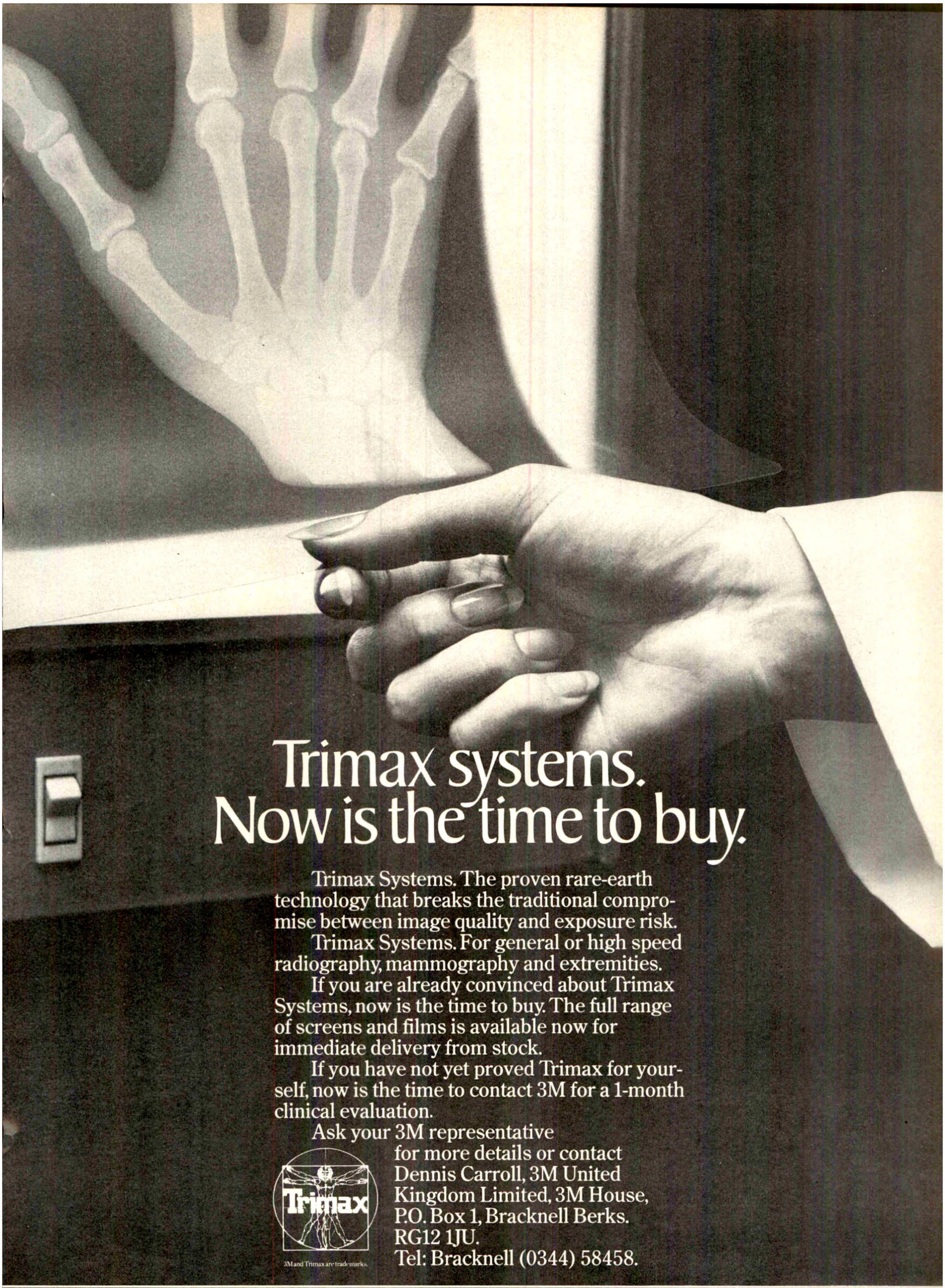

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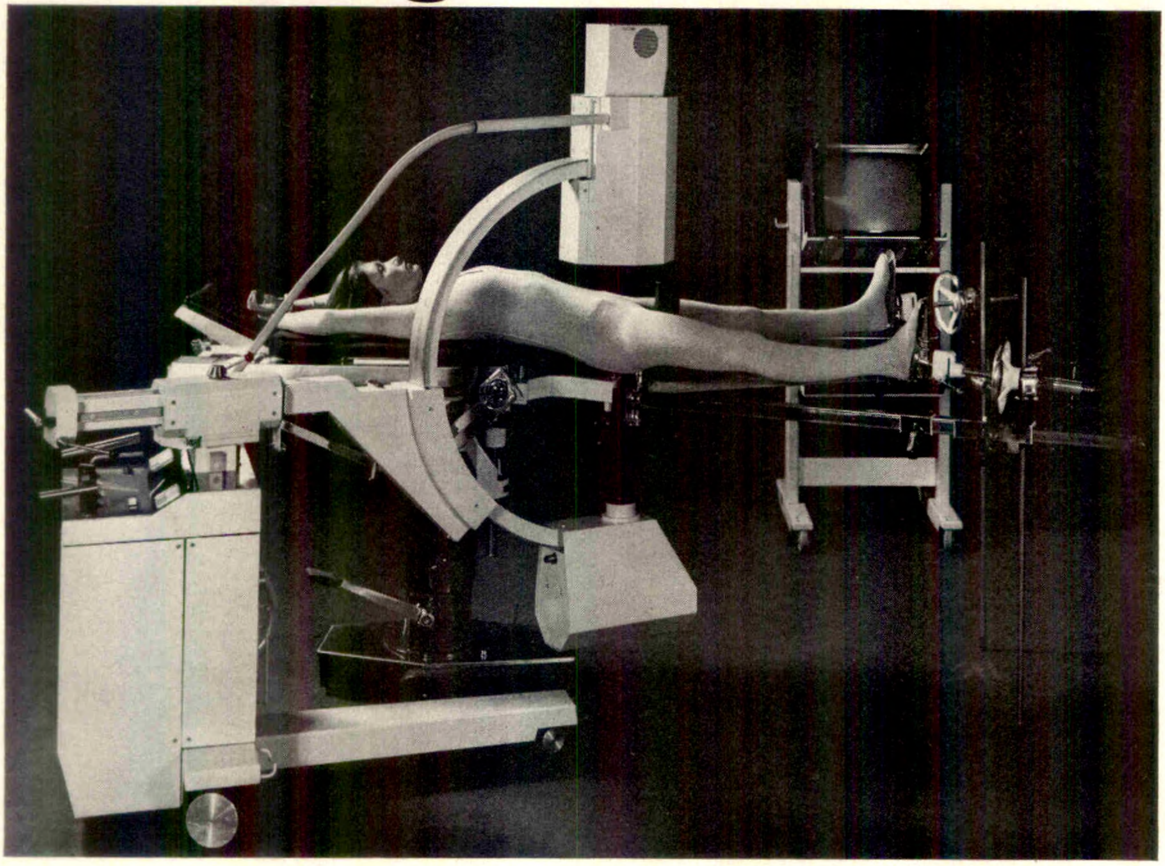

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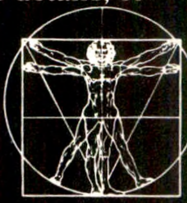

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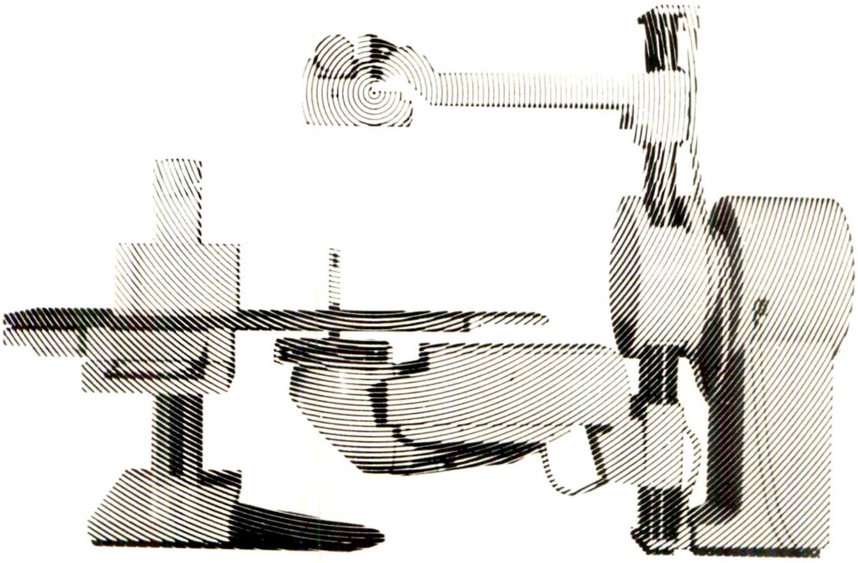

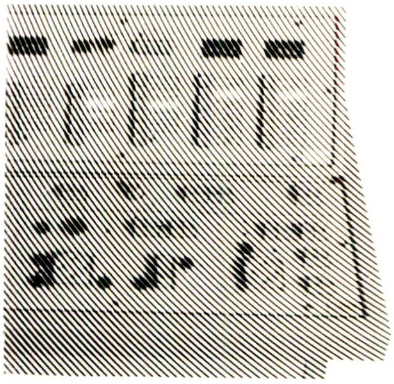

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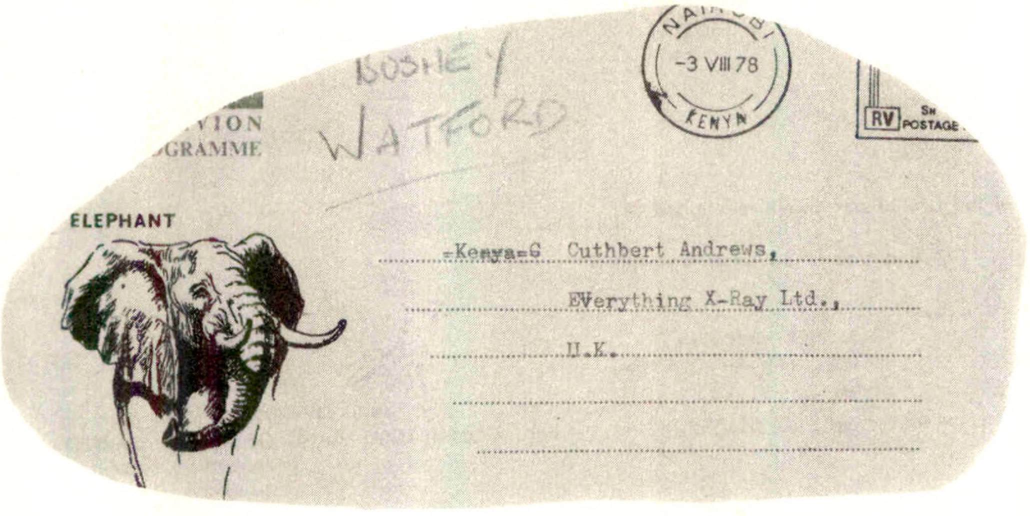

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The British Journal of Radiology

Review article

Radiation effects on pre-natal development and their radiological significance

By R. H. Mole

Medical Research Council, Radiobiology Unit, Harwell, Didcot, Oxon OX11 0RD

(*Received March, 1978 and in revised form September, 1978*)

Abstract

The evidence relating to pre-natal radiation exposure and the subsequent occurrence of malformations and cancer suggests that the overall risk lies in the range 0–1 cases per 1000 irradiated by one rad *in utero* in the first four months of pregnancy. The natural level of occurrence of serious handicaps in average pregnancies is at least 30 times higher. Is the much lower probability of radiation-induced harm sufficiently high to justify (a) concern when a woman who has been irradiated is found to have been pregnant at that time, or (b) the maintenance of restrictions on medical uses of ionizing radiation in women in the reproductive age, such as the ten day rule?

There is now a widespread climate of opinion which takes it as established almost beyond doubt that radiation exposure of the human embryo in its early stages of development is likely to be positively harmful. The conclusions of a recent survey of clinical and experimental information (UNSCEAR, 1977, Report of the United Nations Scientific Committee on the Effects of Atomic Radiation Chap. II and Annex J) could reinforce this opinion. However a careful reading shows that this survey contains many mistakes, both of fact and of inference.

Furthermore there seems to be enough information from irradiated pregnant women to provide provisional estimates of the risk per rad to the embryo or fetus at low levels of exposure such as those involved in diagnostic radiography. The details and a critical review of relevant parts of the UNSCEAR document are set out in an Appendix. The conclusions about the risk estimates are summarized in Table I which may be of practical value when considering whether the so-called ten day rule is justified and whether there is a cause for anxiety in the case of a pregnant woman who is dicovered to have been irradiated when not known to be pregnant. Since there may be wide variations in the purpose of radiographic examinations and the technique with which they may be performed, risk estimates have to be stated in terms of embryonic or fetal dose* and made use of in terms of embryonic or fetal dose per examination. Wherever radiographic examination is stated or implied, the term is intended to include examination utilizing radionuclides also.

This review is primarily concerned with the effects of irradiation received in the first four months of pregnancy. The kinds of risk are:

1. Death of the developing embryo during a short period following the exposure to radiation. This may be a risk for the early embryo irradiated during the first few weeks after conception but much less so for older embryos or the fetus. It is believed, as a result of experimental work confirmed by scattered observations in man, that the lethal dose of radiation is increased markedly at later stages of development.
2. Birth of a malformed child. Sensitivity to a particular malformation is greatest at a particular stage of development, varying with type of malformation and corresponding to the laying down of the primordium for the part which becomes malformed, *i.e.* to the relevant stage of "organogenesis". Thus the very early embryo and the later part of the fetal stage are less at risk than the developing embryo and the early fetus.

Maldevelopment of the brain seems to be much the commonest and most important malformation in the human species. (In experimental animals the most easily detected effects are minor structural abnormalities of bone).

Reprints of this review article may be obtained from The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG at a cost of 75p each; remittance with order please.

*In the human species the accepted convention is that the embryonic period lasts from 0–60 days gestational age and the fetal period from 9–39 weeks gestational age.

TABLE I

NATURAL PREVALENCE OF CONGENITALLY DETERMINED HANDICAPS AND OF CHILDHOOD CANCER WITH ESTIMATES OF ADDITIONAL CASES WHICH WOULD FOLLOW EMBRYONIC OR FETAL EXPOSURE TO A TISSUE DOSE OF FIVE RAD OF LOW LET RADIATION

		No. per 1000	Denominator	Notes
Congenital malformations and other handicaps excluding consequences of accidental trauma	*United Kingdom*			
	Causing still-births and deaths in the first year of life	8	all births	Equivalent to about one-quarter of the total still-births and infant deaths (Forfar, 1973).
	Potentially lethal or handicapping malformtions (excluding Down's syndrome) diagnosed perinatally	24	all births	Leck (1977) Mental retardation and idiopathic epilepsy not identifiable at birth were not included
	Congenital malformations discovered by the second anniversary of birth (including Down's syndrome)	35	all births	For a defined area in South Wales (Lowe, 1972)
	Canada: British Columbia			
	Handicaps of all kinds	90	live births	From a province-wide Registry for Handicapped Children and Adults (Trimble and Doughty, 1974, also cited in UNSCEAR 1977 Annex H)
Perinatal mortality	*United Kingdom*			
	Natural prevalence (all causes)	23–25	all births	Forfar (1973)
	After exposure to X or γ rays of 1–4 month embryo or fetus: additional cases after five rad tissue dose (inferred)	0–1	all births	see text of Appendix
Mortality between 1st and 10th birthdays	Total of deaths from all causes	4–5	alive at 1 year	England and Wales 1970s (Registrar-General)
Mental retardation in adolescence	*United Kingdom*			
	Natural prevalence of severe sub-normality (SSN)	4–5	alive at 15–19 years	Kushlick and Blunden (1974)
	Additional prevalence of less severe subnormality but requiring continued care or support	a few		see text of Appendix
	Japan: Hiroshima qnd Nagasaki			
	In the unirradiated	8–10	alive at 17 years old	80% Poisson confidence limits 5–14 } see text and Blot and Miller (1973)
	After exposure to γ rays as 1–4 month embryo with average tissue dose = 50 rad	0		80% Poisson confidence limits 0–30 } see text and Blot and Miller (1973)
	Inferred excess { caused by 50 rad	0–25		see text of Appendix
	Inferred excess { expected from 5 rad	0–1		
Malignant disease before the 10th birthday	*United Kingdom*			
	Natural prevalence	about half	all live births	see text of Appendix
	After exposure to X-rays of 1–4 month embryo			
	Inferred excess after { 50 rad tissue dose	about 50		
	Inferred excess after { 5 rad tissue dose	about 5		

3. An increased frequency of malignant disease in childhood.

The frequencies of occurrence of the various risks have to be balanced against the medical desirability of the associated radiographic examinations: general principles involved in striking this balance are briefly discussed at the end of the Appendix.

Risk estimates for pre-natal radiation exposure in man

No risk estimate is available for embryonic death caused by ionizing radiation. Embryonic death early in pregnancy is commonly not recognized by the potential mother. Recent investigations of spontaneous abortions and of abortions induced for other reasons than supposed radiation damage have revealed a high frequency of chromosomal abnormalities in the spontaneous cases. In a similar way embryonic death after over-exposure to radiation is likely to be a mechanism which reduces the likelihood of development of a malformed child. The most important consideration is the generally accepted value judgement that early embryonic losses are of little personal or social concern. Possibly this attitude is less valid in the case of the few who are much less fertile than average.

Malformations of a given part of the body may be of very varying degrees of severity, and malformations of different parts may vary greatly in their significance to the mother and the child. In the United Kingdom at the present time about a quarter of all still births and of all deaths in the first week after birth are caused by congenital abnormalities and the death rate in this peri-natal period provides a useful index when considering the rate of induction of the severest categories of malformations. Brain damage of a degree which is severely handicapping will commonly not be recognized until sometime after birth and its frequency in adolescence is a second useful index. Estimates of risk can be derived for peri-natal mortality and for mental retardation in teenagers. Each lies in the range 0 to 1 per 1000 for an embryonic or fetal tissue dose of five rad of low LET radiation. The natural rates per 1000 in UK are about 25 for peri-natal mortality and greater than four for severe mental retardation.

Mortality after the peri-natal period and up to 24 years of age was not increased in Japanese bomb survivors irradiated *in utero*, even at sublethal doses.

No estimate of risk is available for non-lethal handicaps originating outside the central nervous system.

It must be recognized that there is considerable uncertainty about the numerical values of the stated estimates of risk (see Appendix). However, the ranges quoted in Table I are intended to give an impression of the overall confidence limits of the estimates and no allowance has been made for the considerable possibility that there would be a threshold for tissue damage, and therefore for radiation dose, below which many malformations would not occur. This concept of a threshold is a well-accepted general principle in teratogenesis and there is no reason to expect that radiation-induced malformations would provide an exception.

Thus the effect of an X-ray dose of five rad to the embryonic or fetal tissues in inducing congenitally determined handicaps, lethal and non-lethal taken together, would seem to be less than two cases per 1000 births, probably less than one per 1000. There is no reason arising from experimental work, clinical observations on the mentally defective in general, or the surveys of Japanese bomb survivors in particular, to think that non-lethal handicaps originating outside the central nervous system would occur sufficiently frequently to falsify this conclusion. A small reduction in head circumference or in stature without obvious mental retardation seemed to be a little more frequently induced at a given radiation dose than mental retardation itself (cf. Miller and Blot, 1972, and Blot and Miller, 1973) and this can be included in the category of non-lethal handicap of the previous sentence. Alternatively it need not be regarded as a handicap at all.

A medical diagnostic exposure giving a tissue dose of five rad to the embryo or fetus in the first trimester would increase the expectation of cancer in childhood by as much perhaps as ten-fold (Table I and Appendix). A statement in this form may seem to imply a substantial risk. However, the absolute additional risk might be about five in 1000. This estimate is higher than might be expected from published information (Mole, 1974; UNSCEAR, 1972, 1977) because it includes an allowance for the possibility of an increased sensitivity in the first trimester as compared with later stages of pregnancy. It is possibly too high rather than too low (see Appendix). Even at early stages of pregnancy the cancer risk seems to be greater than the teratogenic risk (as suggested before by Mole, 1976).

The preceding numerical assessments of risk are given in terms of a five rad fetal dose (Table I). Putting on one side the question of a threshold, it is radiobiologically reasonable to suggest that risks from smaller doses will be lower simply in proportion to magnitude of dose. It may thus be concluded that the combined risk of cancer plus serious malformations is in the range 0–1 cases per 1000 for an embryonic or fetal tissue dose of one rad received in the first four months of gestation. A dose of one rad is a reasonably representative value for embryonic or fetal exposure in many radiographic examinations which involve abdominal exposure of a pregnant woman (ICRP, 1970; UNSCEAR, 1972; NCRP, 1977b). Some perspective may be provided by considering the practice of genetic counselling (Emery, 1975). The levels of risk considered there range upwards from the overall risk in the average pregnancy for birth of a child with severe handicap, that is, upwards from about 1/30 (cf. Table I).

The estimates of risk cited were derived from evidence concerning brief exposures and are therefore applicable to diagnostic radiography but not necessarily to examinations involving administration of radionuclides. There is as yet no direct evidence in man or in experimental animals about the influence of protraction in modifying the effects of a tissue dose of a few rads. Simple radiobiological theory suggests quite strongly that at this level of dose there would be no influence on cancer induction regarded as a process based on change in a single cell. Therefore whether or not protraction reduces malformations it would not have a practically important influence in reducing the overall risk, because, as noted above, most of this is cancer induction.

Unwitting radiation exposure of a human embryo at an early stage of development

A woman in the early stages of pregnancy who comes to realize, sometimes rather suddenly, that her child-to-be was irradiated in the course of a medical examination conducted a few days or weeks earlier, may find herself in an emotional crisis. On the one hand she way want her child badly; on the other she may feel that her child is now almost bound to be seriously malformed. In the nature of the case practical decisions, for instance about whether to leave the pregnancy to take its natural course or to arrange an abortion, may have to be taken without much time for reflection. There is not the possibility, the value of which is so much emphasized in genetic counselling (Emery, 1975), of postponing consideration of decisions for the future until parents have had some time to recover from the upset and confusion associated with hearing for the first time of the existence of the problem. But in either case the essential counselling must be based on dependable information on the magnitude of the risk, both absolutely and also relative to the unavoidable risk of bearing an abnormal child in the normal course of an ordinary pregnancy; for instance, had the irradiated woman not had the medical examination or examinations in question.

Table I provides numerical information about the kinds of risks which are likely to be uppermost in the imagination of such a woman and of her medical advisers, both as they occur normally and after exposure to radiation. In the natural course of ordinary pregnancies the risk of bearing a clearly abnormal child may seem quite high but is in fact as stated. As the entries in Table I show, the numerical level of the risk depends on how abnormality is defined and when it is measured.

A further matter to be mentioned is the risk to the mother of a decision to perform an abortion, a risk which must be set in the balance against any advantage this might bring. In the few cases that have come to my attention—and they are certainly selected since most fathers or mothers or both were medically qualified or nurses or other medical workers—there have been what can only be called devastating emotional or mental sequelae, far greater than for abortion under more normal circumstances. The radiographic exposures in question were commonly performed as part of a series of investigations into the reasons for failure to conceive. In such circumstances extreme anxiety and guilt seem only too likely consequences of finding oneself or one's wife pregnant and then sacrificing the child.

A practical suggestion is to put the burden of counselling into the hands of one of the NHS genetic advisory centres (Emery, 1975). Genetic counsellors have the experience which would help in this work and they have the great advantage that they are most unlikely to have been involved in the radiographic or other investigations which have led to the situation in which a couple may find themselves. The latter cannot regard the radiologist responsible for the radiography as wholly neutral and on their side. Yet so often it seems to be the radiologist or the hospital physicist who seeks advice about the possible harm that radiation exposure of a developing fetus might do. In fact one purpose of this article is to provide the factual background which may be used in counselling by those who are not familiar with radiobiological problems.

Restrictions on planned exposures of potentially pregnant women in the course of medical examinations by X rays or radionuclides

In 1966 ICRP made a recommendation (para. 76) in the following terms: "The Commission wishes to call attention to reports of embryonic and fetal sensitivity to ionizing radiation and to emphasize that the possibility of pregnancy must be taken into account by the attending physician when deciding on radiological examinations that involve the lower abdomen and pelvis of women of reproductive capacity. The Commission also wishes to point out the the ten-day interval following the onset of menstruation is the time when it is most improbable that such women could be pregnant. Therefore, it is recommended that all radiological examinations of the lower abdomen and pelvis of women of reproductive capacity *that are not of importance in connection with the immediate illness of the patient*, be limited in time to this period when pregnancy is improbable. *The examinations that it will be appropriate to delay until the onset of the next menstruation are the few that could without detriment be postponed until the conclusion of a pregnancy or at least until its latter half*". I have italicized the parts of this recommendation (NOT rule) which are usually overlooked. It was clearly envisaged that the risk to the fetus will usually count less in the balance of risk and benefit than the medical need for radiography of the mother except for the *few* examinations which could be postponed for some considerable time (to the latter half of the pregnancy or until after its end, but this phraseology has now been overtaken by our increasing understanding of the nature and magnitude of the fetal risk and how it is modified by stage of fetal development).

This ICRP recommendation which presumably relates to a minority of radiographic examinations, those that can without detriment be postponed, was carefully worded to avoid suggesting a rule and in the expectation that professional judgement would always be the decisive factor. Nevertheless the ICRP recommendation has been extensively misused to justify a system of general restrictions on radiography of women of reproductive age, which has been given the name "the ten day rule". This has been supported by the argument that any arrangements which reduce the chance of occurrence of even one case of childhood cancer or fetal maldevelopment are thereby justified. This is an emotional statement to which at first sight no exception can be taken but which in fact does not bear logical examination. If the price of the restriction was relatively high, say loss of life by more than one woman of reproductive age, would the absolute justification remain? Clearly the problem of whether and what restrictions there should be on radiographic examinations of possibly pregnant women is a typical example to which the principles of cost-benefit analysis apply. Part of the cost is illustrated in the risk levels of cancer and maldevelopment shown in Table I.

It is almost certainly a valid comment that a decade ago the risk of inducing malformations and cancer per radiographic examination was believed to be much higher than is suggested by the facts as they are known now and summarized in Table I and discussed in the following Appendix. Since 1966 the fetal dose per maternal examination has certainly been reduced by the wider adoption of improved techniques and the risk per unit dose also appears less than had been imagined. At what level of risk should effort to reduce risk cease? Certainly when the additional effort and resources required to reduce risk further could be more beneficially applied in some other direction (see Appendix, final sections). This review is not the place to go into any further detail of what is unavoidably a most complex matter of judgement. It is not possible to imagine that there could be an objective decision to which all would agree because it depended simply on "facts". But the risks to the developing embryo or fetus of maternal X-ray examinations are by no means so large as obviously to justify the continuation, let alone an extended application, of the ten day rule as set out in the Code of Practice for the Protection of Persons against Ionizing Radiation arising from Medical and Dental Use (HMSO, 1972). Indeed this "rule" may not seem to be justified as it stands by the revised Recommendations of ICRP (1977). Paragraph 206 there runs: "Because of the risk of radiation injury to any embryo or fetus, the possibility of pregnancy is one of the factors to be considered in deciding whether to make a radiological examination involving the lower abdomen in a woman of reproductive capacity. Although such an examination is least likely to pose any hazard to a developing embryo if carried out during the ten day interval following the onset of menstruation, attention should always be paid to details of radiological technique that would ensure minimization of exposure to any embryo or fetus that may be present, whether or not the woman is known to be pregnant". Surely there is a need to reconsider the ten day rule and, if it is to be retained, to justify it anew.

A PERSONAL COMMENT

It is acknowledged that the quantitative estimates of the various risks to the irradiated embryo or fetus have varying degrees of reliability. They suggest, nevertheless, that the harm caused to a developing human conceptus by ordinary medical radiography of a mother-to-be is much smaller than the unavoidable risks to the unirradiated embryo of simply developing into a human being, indeed so much smaller that a mother-to-be who has been radiographed should have no reason for additional anxiety. It is to be feared that the extreme anxiety which some pregnant and irradiated women experience at the present time is engendered by apprehensions derived partly from inaccurate accounts of the facts (such as that in Annex J, UNSCEAR, 1977) and partly from well-intentioned attempts on the part of the medical profession to limit the frequency of radiographic exposure of the embryo or fetus.

SUMMARY

The overall risk of serious radiation-induced harm following exposure of the developing embryo or fetus to diagnostic X-ray exposures in the first trimester of pregnancy is most probably in the range 0–1 cases per 1000 receiving one rad tissue dose. The 0–1 cases would mostly be cancer in childhood: severe mental retardation would be less common than cancer.

The natural expectation for the birth of a markedly handicapped child at the end of a normal pregnancy is about 1/30. The risk from medical diagnostic procedures would seem to be at least 30 times smaller than this. Concern over radiographic exposure of the developing embryo or fetus may be unnecessarily heightened by the existence of measures intended to reduce the possibility of exposure. Are these justified?

APPENDIX

A REVIEW OF SELECTED PARTS OF UNSCEAR (1977) CHAPTER II AND ANNEX J

The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) periodically publishes reviews of the current state of knowledge. Its 1977 report contained a short summary on Radiation Effects on Prenatal Development (UNSCEAR, 1977, Chap. IIC) and a long and comprehensive review of the clinical and experimental observations on Developmental Effects of Irradiation *in utero* (loc. cit.: Annex J). The first conclusion of the summary is important. "Very few human data are available on which to base any quantitative estimate of risks from radiation" for exposure at pre-natal stages of development "and it is clear that values derived from animal studies cannot be directly applied to man" (UNSCEAR, Chap. II, para. 30). Unfortunately other statements in the summary may well mislead a reader seeking guidance on the effects of radiation exposure on the human embryo or fetus, especially if his interest is in the possible effects of tissue doses in the range 0–25 rad. This is chiefly because most of the relevant human information comes from Japanese bomb survivors irradiated *in utero* and insufficient attention was paid in Chap. II to the important differences between Hiroshima and Nagasaki, which may be attributed to the neutron component of the exposure of Hiroshima. At Nagasaki irradiation was almost wholly by γ rays and it is this low LET exposure which is more relevant to practical problems in radiological protection and to the taxing and emotionally demanding problem of providing appropriate counselling when a woman who has received abdominal diagnostic radiography is subsequently found to have been in an early stage of pregnancy at the time.

Annex J of the 1977 UNSCEAR Report, Developmental Effects of Irradiation *in utero* (paras 1–353), reviews what is agreed to be a rather large literature (Annex J, para. 335) but unfortunately it too is misleading because of its serious errors, for example in summarizing human information on diagnostic radiology, and because of the same failure to make a clear enough distinction between observations at Hiroshima and Nagasaki.

Bomb survivors in Japan

The observations are summarized: "There was an increased incidence of microcephaly and mental deficiency as a function of dose at Nagasaki following exposures within 3–17 weeks of gestation" (Chap. II, para. 35). This sentence contains two serious mistakes. The observations were about "small head size" not microcephaly (see Risk Estimate for Mental Retardation below) and, with this correction, the sentence is an accurate statement about Hiroshima but not about Nagasaki. At Nagasaki cases of "small head size" and mental retardation were too few for an influence of gestational age to be more than suggestive and then only at the highest exposures (Miller and Blot, 1972; Blot and Miller, 1973). In fact there was a striking difference in dose effectiveness between the two cities for both kinds of effect. "Small head size' was not seen at Nagasaki except at kerma exceeding 150 rad, but at Hiroshima the lowest effective kerma was 10–19 rad (Annex J, para. 145). At kerma of 200–299 rad the increase in incidence of mental retardation as compared with a control sample was 100+ fold at Hiroshima and 12 fold at Nagasaki (Annex J, para. 146). There was some increase at lower values of kerma at Hiroshima but none at Nagasaki (Fig. 1). It may be misleading to think that mental retardation at Nagasaki was a function of dose since the normal interpretation of that phrase would exclude a marked change in dose-effectiveness at 200 rad kerma. The findings were 0/78 at 10–199 rad (average about 60 rad) but 4/12 at 200+ rad (average perhaps 300 rad) and 4/246 for controls (Blot and Miller, 1973).*

Chap. II (para. 38) stated "Japanese exposed *in utero* as a result of A-bomb explosions in Hiroshima and Nagasaki at doses exceeding 50 rad have shown, at the age of 17 years, clear evidence of reduction in body size". This is a true statement of what is in Reference 368 of Annex J but Annex J itself (para. 203) refers to doses above and below 25 rad (not 50 rad) and gave as the reference for this a report on mortality (not body size) which does not subdivide dose at a 25 rad dividing line. From a practical view point the important finding in Reference 368 is that there was no consistent difference in five different criteria of body size between those exposed to 10–50 rad at Hiroshima or Nagasaki, those exposed to one rad or less, and those whose parents were not in either city at the time of the bombing. This is not brought out in Annex J of Chap. II. The 50+ rad group in which effects on growth were shown had a mean kerma at Nagasaki of about 150 rad (Annex J, Reference 48).

The only risk estimate for man given in Chap. II (Para. 35) is stated in terms of frequency per rad and is cited from UNSCEAR (1969). No guidance is provided about whether or not the risk estimate is regarded as still valid in 1977. The qualification attached to the estimate "for doses over 50 rad delivered at high dose rates" is likely to be disregarded by many readers since no cautionary phrases are added, not even a hint about the shape of the dose-response curve. In experiments "in the vast majority of cases the malformation incidence has a curvilinear trend with dose" (Annex J, para. 340 (e)). This same paragraph (Annex J, para. 340 (f)) in reference to microcephaly (*sic*), in its most extreme cases accompanied by mental retardation, stated that "Following high acute doses its incidence has been tentatively estimated at around 10^{-3} rad^{-1} with the lowest effective doses

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*"The upper 80% confidence limit for the first mentioned group is 2.3/78 = 29.5 per 1000: the lower 80% confidence limit for controls at Nagasaki is 1.74/246 and for the combined controls at Nagasaki and Hiroshima 5.43/1076 = 5.0 per 1000".

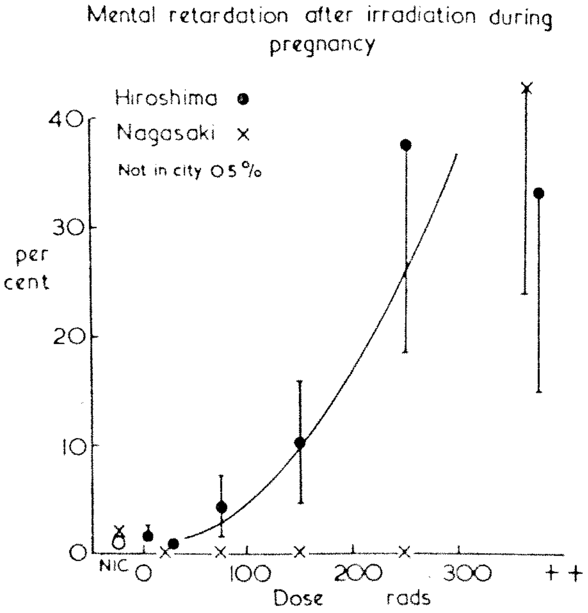

FIG. 1.

Mental retardation after irradiation *in utero* (data of Blot and Miller 1973 on Japanese bomb survivors). The curve shown for Hiroshima is for (dose)^2 (from Mole, 1975). Cases of mental retardation apparently due to identifiable causes other than intra-uterine irradiation have been excluded.

Mental retardation was diagnosed if the child was "unable to perform simple calculations, to make (carry on a) simple conversation, to care for himself, or if he was completely unmanageable or had been institutionalized" (Wood *et al.*, 1967a and b. The word "simple" was omitted from the definition given by Blot and Miller, 1973).

ranging between 10 and 150 rad under different conditions of exposure". Apart from the confusion engendered by stating a linear risk estimate with a "lowest effective dose", the statement misleads because 10 rad refers to exposure at Hiroshima, 150 rad to Nagasaki.

None of the "doses" given in the earlier reports from the Atomic Bomb Casualty Commission (ABCC)* on Japanese survivors irradiated *in utero* are in terms of the current T65D dosimetry system of ABCC. These earlier reports usually classified subgroups according to distance from the bomb hypocentre but occasionally (Annex J, References 48 and 368) stated doses in rads apparently derived from relationships between distance from hypocentre and air doses according to the T57D system but possibly not taking shielding into account. The first report using the T65D system was in UNSCEAR (1969, p. 85, Annex B, Table V) citing doses provided in a personal communication from ABCC but without further details. Later Miller and Blot (1972) and Blot and Miller (1973) used the full T65D kerma system which specifically takes account both of the revision of the nominal power of the Hiroshima bomb and of the shielding of each individual survivor and which is a considerable advance in reliability as compared with earlier dosimetry.

The T65D dosimetry system is in terms of kerma, not absorbed dose in a tissue. The average absorbed dose to the fetus *in utero* may be derived from the maternal kerma by multiplying by a factor less than one. For bomb γ radiation Kerr (1975) suggested a factor of 0.42, and Hashizume and Maruyama (1975) tabulated factors which varied systematically according to developmental age of fetus or embryo, lying in the ranges 0.42–0.66 for the 1st–4th months but 0.32–0.59 for the 7th–9th months of gestation. For present purposes a value of 0.5 will be used and, if this is applied to the values of kerma as stated in the literature and cited by UNSCEAR (1977, Annex J), it may be concluded that fetal doses of at least 100 rad of γ radiation were required to cause a measurable increase in frequency of severe mental retardation and that perhaps somewhat smaller fetal doses, but at least 50–75 rad, were required to cause a measureable degree of reduction in head circumference (cf. Table I in Blot and Miller, 1973 and Table I in Miller and Blot, 1972). There were 78 and 66 subjects respectively without evidence of effect after receiving fetal doses of 5 to 50 or 100 rad, averaging about 40–60 rad.

It is perhaps unfortunate and certainly misleading that UNSCEAR (1977, Annex J, para. 49) should write "Critical re-evaluations of the doses received by the exposed individuals (those *in utero*) were performed at various times" (citing Auxier 1975 and Hashizume and Maruyama, 1975) "but only the most recent reports include reasonably satisfactory dose evaluation" (citing Miller and Blot, 1972). In fact there seems to be no report as yet on frequency of effect in relation to dose based on assessment of dose in fetal tissue. It should also be noted that there are discrepancies between the tabulations of numbers of exposed subjects and of affected subjects between the different accounts of the same investigations (Annex J, References 24, 196, 345, 368). Some but not all of these appear to be the consequence of reassessment of dose. Fortunately the broad conclusions as stated here seem not to be affected.

Diagnostic radiography

The only direct observations on medical exposures (apart from radiotherapy) referred to in Annex J (para. 208) came from a retrospective survey of radiography by Nokkentved (1968, Annex J, Reference 228). Malformations were found in 9.9% of 152 Danish children who had been irradiated in the course of diagnostic procedures (often multiple) and in 9.2% of 143 non-exposed siblings. "The height of children irradiated during the second month of gestation was clearly smaller than control" (Annex J, para. 208). However, this is not what the author said she found. She recorded a higher proportion of children of stature "far below average" amongst those irradiated in the second month of pregnancy than amongst those irradiated in the first, third or fourth month of pregnancy. But "far below average" was not what the words may suggest. It appears to have been defined as less than the expected average height minus one standard deviation, the adjoining category "below average" referring to height between the average height and the average minus one standard deviation. The expectation for a given age and sex, *i.e.* the control value, was taken from a standard paediatric textbook for Scandinavia. The recorded difference between children irradiated in the second month and in the other months of pregnancy was not statistically significant.

Nokkentved (1968) also noted that receipt of drugs during the pregnancy and social class of the mother were each significantly correlated with stature of children. She concluded, without showing how she reached the conclusion, that neither of these factors could be the sole explanation of the "numerous cases of short stature after irradiation in the second month" and that "a somatic effect following irradiation in the 2nd month cannot be ruled out". However, no analysis was made to see if the combined effect of social class and drugs during pregnancy could account for the apparent concentration of cases of short stature in those irradiated in the second month of pregnancy and, as noted above, this concentration of itself was said to be statistically non-significant. Annex J (para. 208) stated: Nokkentved's finding that "the height of the children irradiated during the second month of gestation was clearly smaller than control [*sic*] . . . could not be explained by a number of biological, medical or social factors taken into consideration" and "This study confirms therefore the existence of a growth-retarding effect of irradiation during the second month of pregnancy". It is not possible to accept either of these statements in the UNSCEAR Report as a fair representation of the findings reported by Nokkentved.

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*Since April 1975 the Atomic Bomb Casualty Commission has been replaced by the Radiation Effects Research Foundation (RERF).

A more recent investigation not cited in Annex J (Villumsen, 1970) was a prospective survey of congenital malformations covering a wide range of possible causative factors. No correlation was found between diagnostic X-ray exposure of the abdomen during the first trimester and the frequency of malformation or of reduced head circumference measured post-natally. However, measurements of head circumference and of mental ability at later ages, *e.g.* in adolescence, would be required before Villumsen's results could be compared with those from Japanese bomb survivors.

Radiotherapy

In no case in a literature survey was the probable exposure of the embryo less than 250 R (Annex J, para. 143). Thus the information is not very relevant to considerations of exposures 100 times smaller except for the conclusion that "Irradiation during the pre-implantation stages or at times not exceeding four weeks of gestation can lead to high lethality, but the children that survive are likely to develop normally". Villumsen (1970) found no malformation among seven children whose mothers receive radiotherapy during the first trimester but how many of these received abdominal irradiation was not stated.

Perinatal and later mortality after pre-natal exposure of the developing child

The information on the experience of the Japanese bomb survivors was alluded to quite briefly in UNSCEAR, Annex J (para. 195) but is worth examining in more detail because of its value in practical problems. About one in four of those dying perinatally in U.K. die because of malformations of one kind or another. Perinatal deaths are still-births plus deaths in the first week of post-natal life.

It is understandable that there is no information about the frequencies of potentially lethal malformations amongst children born to mothers during the nine months after the atomic bomb explosions in 1945 at Hiroshima and Nagasaki. During that period there was "confusion of the official vital statistics reporting system" (Kato, 1971) and some death certificates are not available. However, an analysis of mortality rates over the period 1945–1969 has been made utilizing all the available information on those irradiated *in utero* (Kato, 1971). Mortality from all causes at less than one year of age was increased in a radiation dose-dependent manner. There was no effect of radiation exposure on mortality at one to 9 years of age and at ten to 24 years there was a marginally significant increase of mortality with dose (but see below). Analysis of those cases with more detailed information about the cause of or age at death showed that peri-natal mortality increased with increasing radiation exposure and inspection of Kato's Table 6 shows that this was wholly due to excess deaths at maternal kerma of over 180 rad. The perinatal mortality-rate at 40–179 rad was the same as at 0–9 rad. Kato's Table 6 allows a reader to deduce the observed and expected numbers of deaths for all deaths other than perinatal for the sub-population where deaths were known to be from natural causes *i.e.* excluding accidents and unknown causes. The ratio observed/expected was 1.1, 0.7, 0.8, 1.2 and 0.4 respectively for kermas of 0–9, 10–39, 40–179, 180+ rad and unknown magnitude. There was clearly no significant dose-dependent mortality except for perinatal mortality.

When the data were examined according to trimester of exposure, a significant increase with dose in deaths from 0–24 years of age was observed only in those exposed to bomb radiation in the third trimester. Kato (1971) wrote that the dose-associated excess mortality under one year of age "is observed only among children who were in the third trimester" (but gave no data in support of this conclusion). A dose-related effect for exposure in the third trimester suggests that it was mediated through a maternal effect of the bombing. Traumatic injury was excluded (Kato and Keehn, 1966) and it may be suggested that radiation damage by whole-body exposure is the likely maternal factor but there must also have been markedly adverse environmental influences in the aftermath of the bombing. As noted above, all the excess known perinatal mortality was at kerma exceeding 180 rad. These observations of Kato (1971) may be of considerable help in assessing the possible hazards of pre-natal radiation exposure even though they are necessarily based on less than comprehensive information and on relatively small numbers—for example a total of 12 deaths from all known natural causes at kerma over 180 rad, of which five were perinatal.

There was no definitely increased mortality at ages later than the perinatal in a population of 1073 individuals of whom 68 were exposed to over 180 rad with a median value of 293 rad kerma. Thus the hazard of radiation-induced death at ages later than the perinatal from diagnostic X-ray exposure must be very small. The 95% upper Poisson limit for 0/68 is 5.4% and the corresponding limit for five rad fetal dose corresponding to 10 rad kerma (using linearity) would be $0.054 \times \frac{10}{293}$ or 1.8 in 1000. Since all the differences according to radiation exposure are attributable to perinatal, not subsequent, mortality, this value of the risk estimate might be regarded as indicating the upper confidence limit for perinatal mortality.

There was also no statistically established increase in perinatal mortality for exposure in the first trimester. Indeed the data in Kato's Table 7 show that the rate for 0–24 year mortality in the group with a median kerma of zero was slightly greater than for the pooled experience of the three groups with known kerma over 10 rad (and average kerma about 80 rad), 13.5 per 1000 as against 12.6 per 1000. The corresponding rates for the two lower kermas grouped together, 0–49 rad, and the two higher kermas grouped together, over 50 rad, were 12.0 and 17.9 and the difference corresponds to a mortality rate of 0.4 per 1000 per rad.

However, these risk estimates are unrealistically high for exposures to diagnostic X-rays, possibly by an order of magnitude. One main reason is that a linear dose-response has been assumed when the experimental evidence strongly suggests that the response per rad would be curvilinear over the range of doses 5–150 rad (or 10–300 rad kerma). A second main reason is that the great majority of the observations come from Hiroshima, not Nagasaki, and all the evidence there is of prenatal damage in bomb survivors irradiated *in utero* shows that the effectiveness per unit kerma was greater at Hiroshima than at Nagasaki. This was so for "small head size" and mental retardation, as noted, and also for decreased birthweight (Kato and Keehn, 1966). Any deductions which ignore the difference in quality of radiation must inflate considerably the risks from low LET irradiation such as diagnostic X rays. Thus the expectation is (leaving cancer for later discussion) that five rad of X-ray dose to the developing embryo of whatever stage is unlikely to increase perinatal mortality or mortality in childhood and adolescence by as much as one in 1000 at risk.

RISK ESTIMATE FOR MENTAL RETARDATION

The observations on frequency of mental retardation diagnosed in adolescence in relation to level of maternal radiation exposure of Japanese bomb survivors allow an estimate of the risk after five rad of embryonic or fetal tissue dose to be derived in the following manner. The upper 80% Poisson confidence limit for mental retardation after a mean fetal dose of 50 rad was 30 cases per 1000 and the lower 80% limit for effectively zero exposure was five per 1000*. Thus depending on the asymmetry of the distribution, there was a 10–20% probability that the true risk for 50 rad exceeded 30 per 1000 and a corresponding 10% probability that the true risk for zero exposure was less than five per 1000. The probability that 50 rad caused 30–5 = 25 or more cases per 1000 was therefore between the product of $\frac{10}{100} \times \frac{10}{100}$ and $\frac{20}{100} \times \frac{20}{100} = 1$ to 4% so that 25 per 1000 may be regarded as an approximate value for the upper 95% confidence limit of the differences†. It follows that on the linear hypothesis the 95% confidence limits for five rad would be 0–2.5 per 1000 and a better value would be 0–1 per 1000 since the dose response is likely to be curvilinear.

When making use of this information it is important to note that the definition of mental retardation utilized in the Japanese surveys (see legend to Fig. 1) was not in terms which allow easy comparisons with this country. In the UK at the present time those classified as severely sub-normal (SSN) are defined as those with IQ less than 50/55 or untestable and the prevalence of SSN at ages 15–19 is about four in 1000 in England and a little higher in Scotland and Northern Ireland. The prevalence is regarded as fairly stable and largely independent of environmental influences (Kushlick and Blunden, 1974). The rate is about half that for mental 'retardation" in the unirradiated controls in the assessment of Japanese bomb survivors (Blot and Miller, 1973) and the definition of 'mental retardation' used in the Japanese assessments (given in the Figure legend) would suggest that it included some who would be classified in this country as mildly subnormal (MSN) when IQ tests are done (IQ 50/55–70/75), or "feeble-minded" in the now obsolete language of former days.

At age 15–19 the prevalence of MSN may be in the range 3–9 per 1000 (Table 5, Kushlick and Blunden, 1975) although the prevalence of IQ in the range 50/55–70/75 would be much larger. However the prevalence of MSN decreases to about two per 1000 at ages 30+ years (*loc. cit.*) apparently because a substantial proportion of those in the IQ range 50–75 have educational difficulties associated with social factors, not with physical damage. Thus after leaving school many succeed in adapting themselves over the course of a few years to living successfully in the wider community and without the need for special care (Kushlick and Blunden, 1975). The Japanese value for prevalence of 'mental retardation' in the unirradiated of 8–10 per 1000 is thus reasonably close to the British value of 4–5 for SSN plus some addition for MSN needing continuing care. The information from Hiroshima and Nagasaki on increase in mental retardation as a consequence of irradiation *in utero* may be regarded as broadly applicable to this country, at least for the purpose of the comparisons between radiation effects and natural prevalence being made in this paper.

One further matter requiring mention is the greater frequency of "small head size" than of mental retardation in those who had been irradiated *in utero* by bomb radiation (Miller and Blot, 1972). The common paediatric experience is the opposite: that mental retardation occurs with normal head size and that microcephaly nearly always indicates severe mental deficiency. But the contrast may merely reflect the standards used in diagnosis. In the Japanese bomb survivors "head circumference was said to be small if on one or more examinations it was at least two standard deviations below the average for the age and sex of the patient in each city, and was on all previous and subsequent examination at least one standard deviation below the average" (Miller and Blot, 1972). This seems to be a much less stringent requirement than for the clinical diagnosis of microcephaly.

RISK ESTIMATE FOR INDUCTION OF MALIGNANT DISEASE APPEARING IN CHILDHOOD

UNSCEAR (1972) gave an estimate of 230 cases of malignant disease fatal before the tenth birthday per million exposed to antenatal radiography per rad fetal tissue dose for doses in the range 0.2–20 rad. Others have considered that the evidence that antenatal radiography was the cause of the observed increase in malignant disease was contradictory and/or inconclusive (*e.g.* Miller, 1969; 1974). However, more recent views suggest that the contradictions were only apparent, not genuine (Mole, 1974; UNSCEAR, 1977).

In the UK the observed increase in risk, relative to non-irradiated subjects, was substantially greater for irradiation in the first trimester than in the second or third trimester, but in the first trimester the mean number of films per case was also more than doubled (Table XII in Bithell and Stewart, 1975). Such an increase in films per examination is to be expected since radiographic examinations in the first trimester are very rarely for obstetric reasons. Nevertheless, the risk per film appeared to be 7–8 times greater in the first trimester than in the second and third (with wide confidence limits of 2–30 times). However, the first trimester data may seem highly selected: there were only four controls (*i.e.* living children matched with cancer deaths) compared with 38 cases (*i.e.* children dead with cancer). Moreover, there were no controls at all for radiography in the first two months of pregnancy. At their face value the observations might be regarded as suggesting an exceedingly high sensitivity in the first two months and a sensitivity in the third month about three times that in later months. But there is no confirmation of a strikingly high cancer rate after radiography in the first trimester in MacMahon's USA observations (1962).

For the present purposes the risk of cancer induction in the first trimester will be taken to be 10^{-3} per rad, about five times higher than in the second and third trimesters but with no implication that the risk is believed to be really as high as that. For fetal doses as high as 50 rad the risk will be substantially smaller than expected from simple proportionality when the hypothesis is that induction is linear with dose (Mole, 1974), but not necessarily so if induction is according to a power function of dose. The entry for 50 rad in Table I therefore has an additional uncertainty.

EXPERIMENTAL INFORMATION ON RADIATION-INDUCED TERATOGENESIS BY 5 R

In the reviews by UNSCEAR and others on experimental findings in radiation teratogenesis much attention has been given to the question of whether exposure to 5 R of X or γ rays does or does not produce a measurable effect. Annex J (UNSCEAR, 1977) provided "an updated summary" in the form of a Table entitled "Synopsis of the lowest teratogenic doses observed in mouse and rat" (para. 290, Table 5). However, it may be noted that only two of the 21 entries were published in the ten years before 1977 and that half the entries antedate 1960: clearly there has been little recent effort in this field. Possibly the concept of a "lowest teratogenic dose" is not a fruitful one for experiments and, if it is uppermost in an experimenter's mind, must make it difficult to examine control and irradiated material for the presence of abnormalities with the same degree of care. Precautions to avoid bias in scoring low frequencies of abnormality are commonly not mentioned in experimental reports. Moreover a table like Table 5 in UNSCEAR Annex

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*See footnote on page 95.

†No exact method for the estimation of the confidence limits of the difference between the means of two Poisson distributions is known. Using the normal approximation with a correction for continuity the upper 95% confidence limit for the difference between those at Nagasaki receiving 50 rad γ embryonic tissue dose and controls (0–5 rad embryonic tissue dose) was 30–31 per 1000 when the comparison was made with Nagasaki controls and 20–22 per 1000 when the comparison was made with the combined controls from Hiroshima and Nagasaki (D. H. Papworth personal communication).

J cannot present negative findings which may be as important as positive when considering the possible effects of low doses.

There are seven entries in the UNSCEAR table with 5 R given as the "lowest teratogenic" exposure, all relating to mice. These will be discussed in turn and all will be seen to be unreliable. Two entries are mistakes since the effect observed was embryonic resorption (death), not teratogenesis. The entry for polydactilia misrepresents the conclusions of the author who is cited (Reference 231). Ohzu (1965) stated that hindfoot polydactyly was unlikely to have been induced by X-irradiation ($P=0.2$ for difference from controls of the combined information from 5, 15 and 25 R). Fore-foot polydactyly had a high frequency in controls and was increased significantly only after 5 R ($P=0.025$), not after 15 or 25 R.

The remaining four entries all come from the work of a single author (Jacobsen, 1968, Reference 136) who manifestly conducted and analyzed his experimental work very carefully. However hydramnios was recorded as present or absent without measurement of fluid volume and was no more frequent after 20 R than after 5 R, rendering this determinant of radiation effect of doubtful value, as the author himself realized. The association between hydramnios and malformations is well-known and it would have been essential to take precautions to avoid bias in recording the presence of hydramnios in slight excess in irradiated dams.

Decrease in litter weight in the winter was also cited in the UNSCEAR Table as an effect of 5 R. Jacobsen (1968) actually wrote "in the winter a tendency to diminished values of litter weight is also seen after 5 R dose, in the summer . . . a tendency to increased weight following exposure to 5 R" and gave no indication or the statistical significance of the 2% winter reduction of 3% summer increase. The overall difference in litter weight, taking the control as the base-line, was +0.4% after 5 R, −4.4% after 20 R and −39% after 100 R, so that quite clearly the deleterious effect recorded in Table 5, UNSCEAR Annex J as following 5 R did not really occur.

The other two entries in this Table dealing with Jacobsen's work refer to decreasing tail length and increasing frequency of other skeletal defects (when summed over skeletal regions) in the 18-day old embryos. In Tables 47–51 of Jacobsen (1968) there are 13 comparisons of frequencies of skeletal defects with a clear effect of 5 R as compared with controls but only in six of these was the effect of 20 R clearly greater than the effect of 5 R. Inevitably it must be regarded as unfortunate that there are no explicit descriptions of precautions against the possibility of unconscious bias when making the observations.

In all experimental work using polytocous species like rodents, in which embryonic death and resorption are increased by exposure to ionizing radiation, there is always the possibility that effects in the surviving embryos are the result of a change in the intra-uterine environment and are thus indirectly, not directly, caused by the radiation (Ohzu, 1965). If so, the evidence would not be applicable to a monotocous species like the human.

There is also a striking quantitative difference between rodents and humans in the dependence of frequency of effect on gestational age. Figures XVIII, XIX and XXI for exencephaly, hydrocephaly and microcephaly in the mouse or rat (Annex J, pp. 680–681) show that, with a fixed and substantial exposure to low LET radiation in the range 150–300 R, the frequency alters from close to zero up to 35–60% and then down to near-zero levels with changes in gestation age of 3–7 days. No similarly dramatic changes in frequency of occurrence with small differences in gestation age have been noted in Japanese bomb survivors or others. The gestational age range over which mental retardation was most easily demonstrable at Hiroshima was 6–15 weeks (Blot and Miller, 1973) and the evidence, limited as it is, is against any special sensitivity within that period (Table II, UNSCEAR, 1969, p. 88). The fact that 6–15, *i.e.*, 9 weeks, is about 23% of the whole human gestational period of 39 weeks, just as 3–7, *i.e.* 4 days, is about 20% of the whole murine gestational period, may provide a rational framework for the understanding of mechanisms of radiation damage to the developing nervous system. However the observation should not be taken to imply that there is a short period of extreme human sensitivity to much smaller doses at some stage within the period 6–15 weeks of gestational age.

Brent (1977) independently reviewed some of the experimental results considered in UNSCEAR, Annex J, and added unpublished observations of his own. He stated that no growth retardation or malformation had been seen at ten rad or less of acute irradiation (*i.e.* brief exposure) in rat or mouse but nevertheless entered the symbol ± for gross malformation in his Table I on effects of ten rad on the rat and mouse. He also stated in his text that there had been no increase in tumour frequency after irradation exposure of the fetus of experimental animals, but entered the symbol ± for tumour induction in his Table I, adding a footnote refering to antenatal radiography of the human.

In the state of knowledge as described in UNSCEAR, Annex J, the conclusion would seen to be that human observations have much greater weight than the experimental results when considering the possible effects of embryonic or fetal doses of the order of 5–10 rad.

ATTITUDES IN THE USA

The value of arranging to perform radiographic examinations of women in the reproductive ages at particular stages of the menstrual cycle has been examined in depth by a group in California (Brown *et al.*, 1976). As well as reviewing the available evidence about risk originating from radiation exposure of the developing embryo or fetus, an attempt was made to compare that risk with what might ensue from exposing as yet unfertilized oocytes. If a woman postpones a pregnancy in order to have a radiographic examination, there will be in principle an added risk originating from radiation-induced mutation of the oocytes from which the postponed conceptus develops. The balance of risk is something that ought to be known if there are to be restrictions on radiographic exposure of potentially pregnant women. The authors have also examined records of radiography in order to discover how many or what proportion of examinations would have to be postponed if something akin to a ten day rule had been in operation. They have been addressing themselves to possibly important aspects of an analysis of the balance between benefit and risk which ought to be made before deciding that a ten day rule ought to be introduced and implemented.

Their findings should be of considerable interest and value when they become generally available. Practical implementation of a ten day rule may be a very different matter in the United Kingdom where there are relatively very few radiological examinations in private offices and where, in the course of ordinary radiological work, the delays between a request for an examination and its performance may be very much longer than in the USA.

The United States National Council on Radiation Protection and Measurements (NCRP) has recently issued two relevant reports. NCRP report 53 (1977a) is a "Review of NCRP Radiation Dose Limits for Embryo and Fetus in Occupationally Exposed Women" and NCRP Report 54 (1977b) is entitled "Medical Radiation Exposure of Pregnant and Potentially Pregnant Women". The major difference between these reports is the consideration offsetting radiation risk from medical radiation exposure "that the medical welfare of both the expectant mother and her unborn child may be jeopardized if the indicated radiological examinations are *not* carried out". It is stated that "the attending physician must retain full discretion to decide each case according to his judgement". NCRP recommends special care in selection of patients in certain cases of diagnostic radiology and nuclear medicine procedures and recommends that it is generally advisable for pre-menopausal patients not to run a risk of pregnancy until two months after the studies are carried out. No reason is given for this latter advice. Presumably the unstated reason is the experimental finding in the laboratory mouse that the mature, fertilizable oocyte is more sensitive to mutation than more primitive stages. But, even so, is the possibility of mutation large enough for it to be a decisive factor?

The risk of abnormality in an unborn child receiving five rad or less is considered to be negligible "when compared to the other risks of pregnancy" and "is significantly increased above control levels only at doses above 15 rad". These statements are not supported by numerical values for estimates of risk nor by reference to human information and appear to be based on experimental work in rodents (some of it with preliminary results only) by three of the five members of the Ad Hoc Committee which prepared the NCRP Report 54 (this made no direct reference to other experimental work). The evidence for induction of malignant disease by antenatal diagnostic radiography is regarded, following Miller (1969, 1974), as inconsistent or contradictory and a special point is made that "thus far, experimental attempts to increase cancer incidence by small doses of radiation to fetuses of animals have failed".

If, in a woman of reproductive age, "a diagnostic examination is deemed advisable for the medical well-being of the patient it should be carried out without delay" with special effort to minimize dose. (Just what "special effort" is intended to imply is not discussed.) "Doses below five rad to the human embryo-fetus are considered by many to represent an acceptable risk when compared to the potential medical benefit of the examination to the patient. In practice, very rarely does a diagnostic examination, including fluoroscopy, result in a dose to the uterus as high as five rad. Therefore, at the five rad level it would rarely be necessary to schedule an *elective* examination of a patient. Others, however, may argue for a lower dose to the embryo-fetus above which scheduling of elective abdominal and pelvis examinations should be required". ("Scheduling" means arranging for an examination at the appropriate time between menstrual periods. An "elective" examination is one which may be postponed and, may, therefore, require scheduling).

PRINCIPLES OF RADIOLOGICAL PROTECTION

When planning for allowable exposures the aim is to optimize the balance between the benefit from the practice which involves radiation exposure and its costs, including the risks arising from the exposure (ICRP, 1977). This is as true of medical uses of radiation as of industrial uses, although in detail the criteria may be different. The recommendation that special care should be observed in relation to diagnostic radiography of women in the reproductive age because of the possibility of irradiation of an embryo in the earlier stages of development (ICRP, 1977, 1966) is a case in point.

Whether the use of radiation is for medical or industrial exposures it is usual to set some dose level which should not be exceeded. This will be zero for an industrial use with a benefit which is regarded as trivial or when the benefit can be obtained by other means with a smaller concomitant cost (including risk). It will also be zero for medical uses if there is an alternative means with smaller cost (including risk), say perhaps ultrasonic methods of examination. When exposure of the fetus is involved, the allowable dose would be zero if the reasons against postponement of radiography of the mother until after delivery of the child are insufficiently strong. Dose limits greater than zero are set for annual occupational exposures. The assumption which determines the dose limit is that no industrial benefit, however large, justifies exposing workers to a risk appreciably greater than the average for the safer industries (ICRP, 1977). Corresponding numerical limits are not set for medical exposure of sick people but the existence of occupational dose limits provides yardsticks against which the hazard of medical exposures may be judged, whether to patients who are seeking help, to apparently healthy persons undergoing screening tests, or to volunteers who participate in experiments (WHO, 1977). The hazard should be taken into account when making decisions, for example to set up a screening service ultilizing radiography or to approve of proposed experiments involving the exposure of volunteers to ionizing radiation. The hazard must be less than the expected benefits but any rational cost-benefit-analysis has to take account of much more than that. Inevitably it is a complex matter in which judgement plays an over-riding part.

Sanctions of various kinds are intended to keep occupational exposures below the recommended dose limits. In practice the existence of these sanctions and of the whole system of radiological protection may often give the impression that something dire is almost bound to happen to the individual whose exposure over a given time period exceeds the dose limit by even a small amount or fraction. However, the dose limit for occupational exposure to radiation has been set by reference to the levels of occupational risk met with in the safer industries and originating from other causes, and therefore it has been set by statistical considerations of the average risk to a population over a working lifetime. This average is based on a wide range of levels of risk for different individuals. By comparison with this the extra risk to an individual of a year's exposure exceeding a dose limit set in terms of annual exposure by a factor of, say, 2–3 may be considered as not of great moment. The extra risk would be 4–6% of that incurred by the hypothetical individual exposed continuously at the dose limit for a period of 50 years, or about 50% extra for the hypothetical individual exposed continuously to one-tenth of the dose limit for 50 years except for the single year in which he received the abnormal exposure under consideration.

Given the range of occupational hazard amongst the different individuals who make up any given industrial population, this degree of extra risk above that which was being accepted anyhow might be regarded as negligible or nearly so. Yet occupational exposure in a given year at a level exceeding the dose limit by a factor of 2–3 usually leads to extensive discussion and concern about whether such an "over-exposed" individual should be allowed to continue with his radiation work and so on. Yet, as ICRP say, the main consequence of this degree of occupational over-exposure should be a careful consideration of how it came about to see if re-organization of work could prevent it in the future. The consequence of such an over-exposure should not be the creation of a climate of feeling in which both the individual himself and others in management, in trade unions and in safety organizations, feel strongly that he has suffered some serious harm.

The latter attitudes need to be avoided also when considering unwitting exposure of an early human embryo in the course of diagnostic radiography or the practice of nuclear medicine. It should be obligatory to make as realistic an assessment of the risk as knowledge allows before embarking on a course of re-assurance, or alternatively, interference with the pregnancy. Similarly a corresponding estimate of risk is required before a rationally based decision can be reached on restriction of exposures to diagnostic radiography. Such estimates were not the basis of the so-called "ten day rule". This takes as its basis the concept that the allowable dose is zero, not because an alternative method of examination is available with a risk less than that of radiography, but because there may be insufficient need, *i.e.* benefit, for the examination to be performed at a particular time. In contrast with the occupational situation, where people are thought of as groups and work (occupational exposure) can be planned, the case of each individual patient requires consideration on its own merits to see if the need (benefit) for (from) a radiographic examination at a particular time outweighs the risk resulting from performance of the examination at that particular time. It is clearly extraordinarily difficult to estimate the degree of benefit to be associated with the performance of a given radiographic examination in a given patient, even with hind-sight, let alone without knowledge of the outcome. If the associated risk is small enough, however, there may be no need to estimate the degree of benefit with any precision.

According to the arguments developed in this paper, the overall risk associated with a tissue dose in the developing embryo or early fetus of one rad would seem to lie in the range 0–1 per 1000 for all sequelae combined, *i.e.* serious malformations and cancer put together. The important judgement is whether or not this is a risk level against which precautions ought to be taken. The judgement should include consideration of the extent to which the stated risk estimate may have been unduly inflated, for example by ignoring the evidence for thresholds for induction of malformations and especially by the choice of the risk value for cancer induction following exposure in the first four months of gestational age. If it is concluded that the risk level is high enough to justify the taking of precautions, there are at least three different courses of action which could be pursued singly or in combination:

(a) improving techniques with the aim of reducing embryonic and fetal dose per examination and thereby reducing risk,

(b) scheduling of examinations so as to reduce the chances that an embryo or fetus would be exposed to radiography,

(c) persuasion and education of doctors in general with the aim of reducing the frequency with which relevant kinds of radiographic examinations are asked for.

Each of these courses of action will reduce the risk in statistical terms, none will guarantee that the risk will be zero, each will cost maintained effort and finance to implement. Which (or which combination of all three) would be the most effort- and cost-effective? And can an answer be given for "radiography" in general or only in terms of specific examinations requested for specific reasons? Moreover, in the UK the effort and cost will almost all be met from the resources of the NHS. There is thus a further question: are there alternative ways of expending the same effort and cost with benefits in other directions and in which direction would the national benefit be maximized?

REFERENCES

Auxier, J. A. A., 1975. 1. Dosimetry A. Physical dose estimates for A-bomb survivors—studies at Oak Ridge, USA. *Journal of Radiation Research, 16, Supplement 1–11.*

Bithell, J. F., and Stewart, A. M., 1975. Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford survey *British Journal of Cancer, 31*, 271–287.

Blot, W. J., and Miller, R. W., 1973. Mental retardation following *in utero* exposure to the atomic bombs of Hiroshima and Nagasaki. *Radiology, 106*, 617–619.

Brent, R. L., 1977. Radiation and other physical agents. In *Handbook of Teratology* (ed. J. G. Wilson and F. C. Fraser), Vol. 1, Chapter 5, pp. 153–223 (Plenum Press, New York).

Brown, R. E., Shaver, J. W., and Lamel, D. A., 1976. *A concept and proposal concerning the radiation exposure of women.* Published by Radiological Health Sciences Education Project, University of California (R.H.S.E.P. Publication No. 874).

Emery, A. E. H., 1975. Genetic counselling. *British Medical Journal, ii*, 219–221.

Forfar, J. O., 1973. Demography, vital statistics and the pattern of disease in childhood. In *Textbook of Paediatrics* (eds. J. O. Forfar and G. C. Arneil), chapter 1, pp.1–32 (Churchill Livingstone, Edinburgh).

Hashizume, T., and Maruyama, T., 1975. 1. Dosimetry B. Physical dose estimates for A-bomb survivors—studies at Chiba, Japan. *Journal of Radiation Research, 16, Supplement*, 12–23.

I.C.R.P., 1966. Recommendations of the International Commission on Radiological Protection. *ICRP Publication 9* (Pergamon Press, Oxford).

1970. Protection of the patient in X-ray diagnoses. *ICRP Publication 16* (Pergamon Press, Oxford).

1977. Recommendations of the International Commission on Radiological Protection. *ICRP Publication, 26* (Pergamon Press, Oxford).

Jacobsen, L., 1968. *Low dose X-irradiation and teratogenesis* (Munksgaard, Copenhagen).

Kato, H., 1971. Mortality in children exposed to the A-bombs while *in utero* 1945–1969. *American Journal of Epidemiology, 93*, 435–442.

Kato, H., and Keehn, R. J., 1966. Mortality in live-born children who were *in utero* at the time of the atomic bombs. Atomic Bomb Casualty Commission Report TR-13-66, ABCC, Hiroshima, Japan.

Kerr, G. D., 1975. Report of liaison studies with the Atomic Bomb Casualty Commission, Hiroshima, Japan, August 20–September 17, 1974. Oak Ridge National Laboratory Report ORNL-TM-4830.

Kushlick, A., and Blunden, R., 1974. The epidemiology of mental subnormality. In *Mental Deficiency: The Changing Outlook* (eds. A. M. Clarke and A. D. B. Clarke), Third Edition, Chapter 3, pp. 31–81, Methuen, London.

Leck, I., 1977. Congenital malformations and childhood neoplasms. *Journal of Medical Genetics, 14*, 321–326.

Lowe, C. R., 1972. Congenital malformations and the problem of their control. *British Medical Journal, ii*, 515–520.

MacMahon, B., 1962. Prenatal X-ray exposure and childhood cancer. *Journal of the National Cancer Institute, 28*, 1173–1191.

Miller, R. W., 1969. Delayed radiation effects in atomic bomb survivors, *Science, 166*, 569–574.

1974. Late radiation effects: status and needs of epidemiologic research. *Environmental Research, 8*, 221–233.

Miller, R. W., and Blot, W. J., 1972. Small head size after *in utero* exposure to atomic radiation. *Lancet, ii*, 784–787.

Mole, R. H., 1974. Antenatal irradiation and childhood cancer: causation or coincidence? *British Journal of Cancer, 30*, 199–208.

1975. Man rems and risk. In *Radiation Protection—Philosophy and Implementation.* International Symposium, Aviemore, Scotland, pp. 23–36. EUR 5397e Commission of the European Communities, Luxembourg.

1976. Antenatal radiography and the ten day rule. *Lancet, i*, 738–739.

N.C.R.P., 1977a. Review of NCRP radiation dose limit for embryo and fetus in occupationally exposed women. *NCRP Report No. 53*, Washington, D.C.

1977b. Medical radiation exposure of pregnant and potentially pregnant women. Recommendations of the National Council on Radiation Protection and Measurements, *NCRP Report No. 54*, Washington, D.C.

Nokkentved, K., 1968. *Effect of Diagnostic Radiation upon the Human Fetus* (Munksgaard, Copenhagen).

Ohzu E., 1965. Effects of low dose X-irradiation on early mouse embryos. *Radiation Research, 26*, 107–113.

Trimble, B. K., and Doughty, J. H., 1974. The amount of hereditary disease in human populations. *Annals of Human Genetics, 38*, 199–223.

UNSCEAR, 1969. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. Official Records of the General Assembly: Twenty-Fourth Session, Supplement No. 13 (A/7613) United Nations,, New York.

1972. Ionizing Radiation: Levels and Effects, Vol. II. Effects. United Nations, New York.

1977. Sources and Effects of Ionizing Radiation. United Nations Scientific Committee on the Effect of Atomic

Radiation 1977 report of the General Assembly, with annexes. United Nations, New York.

Vilumsen, A. L., 1970. *Environmental Factors in Congenital Malformations* (F.A.D.L.s Forlag, Copenhagen).

WHO, 1977. Use of ionizing radiation and radionuclides on human beings for medical research, training and non-medical purposes. *Technical Report Series, 611*, pp. 1–39 (World Health Organization, Geneva).

Wood, J. W., Johnson, K. G., and Omori, Y., 1976a. *In utero* exposure to the Hiroshima atomic bomb. An evaluation of head size and mental retardation: twenty years later. *Pediatrics, 39*, 385–392.

Wood, J. W., Johnson, K. G., Omori, Y., Kawamoto, S., and Keehn, R. J., 1967b. Mental retardation in children exposed *in utero* to the atomic bombs in Hiroshima and Nagasaki. *American Journal of Public Health, 57*, 1381–1390.

Book review

Ultrasonography in obstetrics and gynaecology. By J. C. Hobbins and F. Winsberg. pp. ix+174, illus., 1977 (Williams & Wilkins Co., Baltimore) $21.00.

This is one of a number of new books on ultrasound to have been released recently. It is one of the better ones and is the product of obviously close co-operation between an obstetrician and a radiologist. It contains about 170 pages and is strictly limited in clinical content as indicated by the title. Its approach is logical and analytical. Many practical aspects of scanning are rightly discussed because not only are they important, but they are often ignored and not understood. However, I do not think that the first (albeit short) chapter on the basics of ultrasound adds any weight to the book.

The book's main attraction is the combined clinical-radiological approach which shows a good two way understanding. Each chapter finishes with a good list of references and the book's appendix consists of the essential tables and graphs used in obstetrics ultrasound which have been extracted from leading articles. This is quite excellent.

Unfortunately, the quality of the text is not altogether matched by the quality of the illustrations. Many of the ultrasound films are accompanied by pencil drawings which is often a useful adjunct, but should not be a necessity. Some of the opinions represent a rather American attitude often imposed by the type of equipment used in the early days, *e.g.* many British users would not agree with the statement that 'M-mode echocardiography is too tedius for use in the first trimester'. However, this is compensated for by a good approach to the use of real-time scanners and the value of the various fetal measurements.

On the whole this is an excellent book, easily read and to be recommended.

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Pain in peripheral arteriography—a comparison of a low osmolality contrast medium with a conventional compound

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Abstract

The pain reaction to a new low osmolality contrast agent, sodium-methyl-glucamine-ioxaglate, in comparison to the conventional compound methylglucamine-ioxitalamate was tested and statistically evaluated in 12 patients using the visual analogue scale method. The intensity of pain experienced was significantly smaller following intra-arterial injection of the compound of low osmolality as compared to the conventional contrast agent.

Pain due to the injection of the contrast medium is the most unpleasant side effect of peripheral arteriography. The development of contrast media inducing less pain is therefore of great importance. Modifications of the composition of the presently used tri-iodinated compounds have so far had only minor effects on pain reduction. Recently, contrast media with significantly lowered osmolality, such as non-ionic metrizamide (Almén *et al.*, 1977; Almén and Trägardh, 1973) or a dimer of metrizoate (Björk *et al.*, 1969) were shown to cause considerably fewer painful reactions, less pronounced haemodynamic changes, especially peripheral vasodilatation and reduced general and local toxicity.

The purpose of this study was to test patients' pain reaction to a new contrast agent of low osmolality, sodium-methyl-glucamine-ioxaglate (SMI)‡, in comparison with the conventional compound methylglucamine-ioxitalamate (MI).

Material and Methods

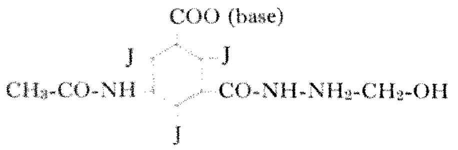
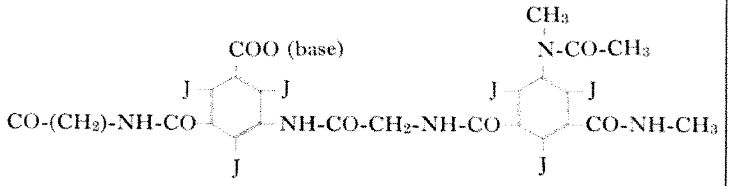
The pain reaction to SMI was tested following intra-arterial injection and compared with the effects of MI. The new monoacidic dimer type of contrast agent contains six iodine atoms instead of three, the osmolality is reduced to one third of that of ioxitalamate (580 mosmol/kg compared with 1430 mosmol/kg) and the iodine content of both agents is equivalent (0.32 g/l compared to 0.30 g/l) (Table I).

Retrograde aortography was performed in 12 patients (eight males, four females, aged 42–81 years, mean age 66 years). All had generalized, occlusive, Fontaine stage II arteriosclerotic disease. Patients under analgesic medication within 48 hours prior to arteriography or suffering from neurological disease (*e.g.* diabetes) were not included in the study.

The patients were informed about the procedure in a standardized manner. The investigator explained that different contrast media would be injected in order to examine the arteries in A.P. and oblique projections. The patients were asked to note the degree of pain felt following every injection by marking a visual analogue scale with a pencil. A new

TABLE I

Tested contrast media

	Methylglucamine ioxitalamate (MI)	Sodium-methylglucamine ioxaglate (SMI)
Chemical structure		 COO (base) CH3 N-CO-CH3 J J J J CO-(CH2)-NH-CO NH-CO-CH2-NH-CO CO-NH-CH3 J J
Salt content (weight/vol.)	66%	59%
Iodine content	30% (0.30 g/l)	32% (0.32 g/l)
Na^+	—	15,5 mval/100 ml
Osmolality	1430 mosmol/kg	580 mosmol/kg
Viscosity (20°)	5,3 cP*	15,7 cP*
Injected volume	80 ml	80 ml

*1 cP $= 10^{-3}$ Nsm^{-2}

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‡R. Guerbet, Paris.

scale was used for each pain-rating in order that the patient was unaware of his previous rating. On this analogue scale the left end of the 100 mm long line signified "no pain" and the right end "unbearable pain". The pain intensities noted by the patient were measured in millimetres.

Following local anaesthesia of the puncture site and percutaneous puncture of the femoral artery, 80 ml of contrast material was injected at a flow rate of 20 ml/sec. Similar injections of 80 ml of saline 0.9% were done as a control study. For the three sequential injections the type of contrast medium or saline injected was selected at random following a complete crossover design. The operator was unaware of the type of solution to be injected. The statistical evaluation was done according to the U-test (Mann-Whitney). The groups were compared one to another in pairs. A non-parametric method was chosen because the measurements were not distributed normally.

RESULTS

The intensity of pain experienced by the 12 consecutive patients was significantly smaller following intra-arterial injection of ioxaglate (SMI) (24.83 ± 26.03 mm) as compared to ioxitalamate (51.08 ± 30.75 mm) ($U = 34.5$, $p < 0.05$). When compared with saline 0.9% (7.65 ± 5.45 mm) ioxitalamate (MI) was significantly more painful ($U = 18.5$, $p < 0.01$), whereas the painful sensations following intra-arterial injection of ioxagate (SMI) were less pronounced ($U = 40$, $p < 0.05$) (Table II).

The quality of arterial contrast filling was identical for both types of contrast medium and the degree of opacification of smaller arteries was the same for both compounds.

DISCUSSION

The assessment of pain is usually based on verbal communication with the patient. However, verbal rating scales have the disadvantage that the subject is forced to translate a feeling or sensation into words. The same word does not necessarily imply the same meaning for each patient. The intervals between word categories do not represent identical steps in pain intensity (Aitken, 1969). The so-called visual analogue scale used in psychosomatic medicine seems to be a method which reflects more precisely the quantity of the patient's actual feelings (Joyce *et al.*, 1975; Ohnhaus and Adler, 1975; Woodfore and Merskey, 1971). The visual analogue scale is also easily managed by the patient and is a convenient method for statistical evaluation. A more objective evaluation of painful sensations recorded by the patient is thus possible. The visual analogue scale method should therefore be used as a standard method when testing pain reactions to contrast media.

This clinical investigation provides statistical confirmation of reports that contrast agents of low osmolality cause significantly less pain than conventional contrast compounds (Almén *et al.*, 1977; Almén and Trägardh, 1973; Björk *et al.*, 1969).

Since the osmolality of ioxaglate (SMI) is less than half that of ioxitalamate (MI), it is interesting to note that the painful sensations following intra-arterial injection of ioxaglate were about half as severe when compared to ioxitalamate. These findings suggest that pain parallels the degree of osmolality of the contrast agent applied (Almén and Trägardh, 1973; Boijsen *et al.*, 1971; Lindgren *et al.*, 1968). For this reason the new monoacidic dimer sodium-methylglucamine-ioxaglate is an ideal contrast material for peripheral arteriography. It causes minimal discomfort to the patient.

TABLE II

VISUAL ANALOGUE SCALE SCORES (MEAN VALUES)

No pain		Unbearable pain	
7.67 ± 5.45 mm			NaCl 0.9%
	24.83 ± 26.03 mm		SMI
		51.08 ± 30.75 mm	MI

REFERENCES

Aitken, R. C. B., 1969. Measurement of feelings using visual analogue scales. *Proceedings of the Royal Society*, *62*, 17–24.

Almén, T., Boisen, E., and Lindell, S. E., 1977. Metrizamide in angiography. *Acta Radiologica Diagnosis*, *18*, 33–38.

Almén, T., and Trägårdh, B., 1973. Effects of non-ionic contrast media on the blood flow through the femoral artery of the dog. *Acta Radiologica*, *Suppl. 335*, 197–202.

Björk, L., Eriksson, V., and Ingelman, B., 1969. Clinical experience with a new type of contrast medium in peripheral arteriography. *American Journal of Roentgenology*, *106*, 418–424.

Boijsen, E., Dahn, I., and Hallböök, T., 1971. Hemodynamic effect of contrast medium in arteriography of the legs. *Acta Radiologica Diagnosis*, *11*, 295–309.

Joyce, C. R. B., Zutshi, D. W., Hrubes, V., and Mason, R. M., 1975. Comparison of fixed interval and visual analogue scales for rating of chronic pain. *European Journal of Clinical Pharmacology*, *8*, 415–420.

Lindgren, P., Saltzman, G. F., and Törnell, G., 1968. Vascular reaction to water-soluble contrast media. *Acta Radiologica Diagnosis*, 7, 152–160.

OHNHAUS, E. E., and ADLER, R., 1975. Methodological problems in the measurement of pain: a comparison between the verbal rating scale and the visual analogue scale. *Pain, 1*, 379–384.

WOODFORE, J. M., and MERSKEY, H., 1971. Correlation between verbal scale and visual analogue scale and pressure algometer. *Journal of Psychosomatic Research, 16*, 173–178.

Book review

Mutagen-induced Chromosome Damage in Man. Edited by H. J. Evans and D. C. Lloyd, pp. 355, 1978 (Edinburgh, University press). £15·00; N.kr98.

Since the previous presentation of data on chromosome damage in human lymphocytes eleven years ago, steady advances have taken place in techniques of chromosome preparation and analysis which have had marked effects on the progress of detection and quantitation of chromosome damage. This symposium which brings these advances up to date contains reviews and recent findings from 37 contributions in various fields of human cytogenetics associated with lymphocyte damage. The main contributions on quantitation of chromosome damage are related to irradiation sources and deal with the present position regarding dose-response relationships after *in vivo* whole or partial body X or γ radiation and comparisons with *in vitro* irradiation of whole blood. The various criteria for analysis of chromosome damage are discussed at some length as to which method of scoring produced the greatest degree of accuracy. The latter part of the symposium deals with the detection of exposure to hazards from chemical mutagens and irradiation sources in the environment and includes long term studies from atomic bomb survivors and patients many years after irradiation treatment. Other contributions concentrate on the economics of methods of testing clastogens in industry and the values of automation in chromosome analysis.

The system used throughout, that of the phytohaemagglutinin stimulation of T-lymphocytes from peripheral blood, presents considerable difficulties both in interpretation and quantitation of results. There is still a considerable lack of information on the behaviour of circulating lymphocytes in the body. This is brought out particularly in the studies on partial body radiation where the frequency of chromosome observations are well below those expected, and although some degree of comparability exists between aberration frequencies after whole body radiation and lymphocytes irradiated *in vitro*, there is still a wide range of variation in the results from different contributions. It is also suggested that to account for these differences different sub-populations of lymphocytes may exist in the circulating blood which have differing radio-sensitivities and which differ in their time of first mitosis after PHA stimulation. Selection for analysis of the first mitotic division after stimulation is a technical difficulty which is discussed at some length particularly in relation to the fixation time of mitotic cells. More recent advances whereby first mitoses can be recognized at any fixation time following bromodeoxyuridine (BUdR) incorporation and harlequin banding processing should eliminate some of these problems and vastly improve quantitation in future. Cell loss *in vivo* is also presented as one contributory factor in the difficulties of comparable analysis.

The survival and detection of different types of chromosome damage many years after irradiation are dealt with by two contributions and it would appear here that the technique of G-banding does not have the advantages which were expected. Although symmetrical translocations and inversions can be detected by banding which would otherwise be missed, it seems that centromeres become "blurred" so that some dicentrics can be undetected in the banding samples.

Analysis of chromosome damage produced by chemical mutagens *in vivo* presents somewhat different problems and is more limited in terms of quantitation. Aberrations which are produced by irradiation in the G_0 circulating lymphocytes are particularly rare following chemical mutagenic treatment. The lesions responsible here are capable of repair and are normally only converted and expressed as chromatid aberrations if affected cells pass through the S period *in vitro* after PHA stimulation. Most of the studies therefore deal with *in vitro* treatment of lymphocytes with suspected mutagens or studies of individuals accidentally exposed to chemical hazards up to a few days or weeks after exposure.

The presence of a significant increase in yield of cells with aberrations is therefore regarded as a criterion of a chemical mutagen. Studies of the frequency of increased sister-chromatid exchanges (SCE) visible in the second mitotic division *in vitro* after BUdR incorporation is proving to be a very useful tool in the investigations of chemical mutagens. These are induced with a wide range of agents at doses well below those required to induce chromosome aberrations. Considerable caution however is still required since aberration production is not necessarily correlated with SCE production in all cases. The increased SCE frequency can, it appears, be detected up to two weeks after accidental exposure to mutagens. A potentially valuable method for chemical agents and pollutants with low mutagenic capability is also described by one contributor, whereby lymphocytes are kept incubated for up to two days in the presence of the agent prior to stimulation with PHA.

This symposium report can be recommended to all those involved in the field of radiation therapy and dosimetry as well as workers in industry dealing with protection from chemical and irradiation hazards.

C. H. OCKEY

1979, *British Journal of Radiology*, *52*, 105–109

Osteochondral fractures of the dome of the talus

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ABSTRACT

Osteochondral fracture of the talar dome is an uncommon lesion occurring after ankle inversion and tearing of the lateral ligaments. This lesion can be overlooked if internal oblique radiographs are not obtained. The value of tomography is discussed. Symptoms may persist for many months if accurate radiographic diagnosis is delayed. Prompt arthrotomy is indicated to prevent post-traumatic arthritis of the ankle joint.

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Osteochondral fracture of the talar dome is an uncommon ankle injury described in the past under a variety of terms: osteochondritis dissecans (DeGinder, 1955; Ray and Coughin, 1947; Roden *et al.*, 1954), transchondral fracture (Davidson *et al.*, 1967), dome fracture (Coltart, 1952; Mukherjee and Young, 1973; Nisbet 1954) and flake fracture. By definition it is a fracture through that part of a bone that is lined with articular cartilage (Davidson *et al.*, 1967).

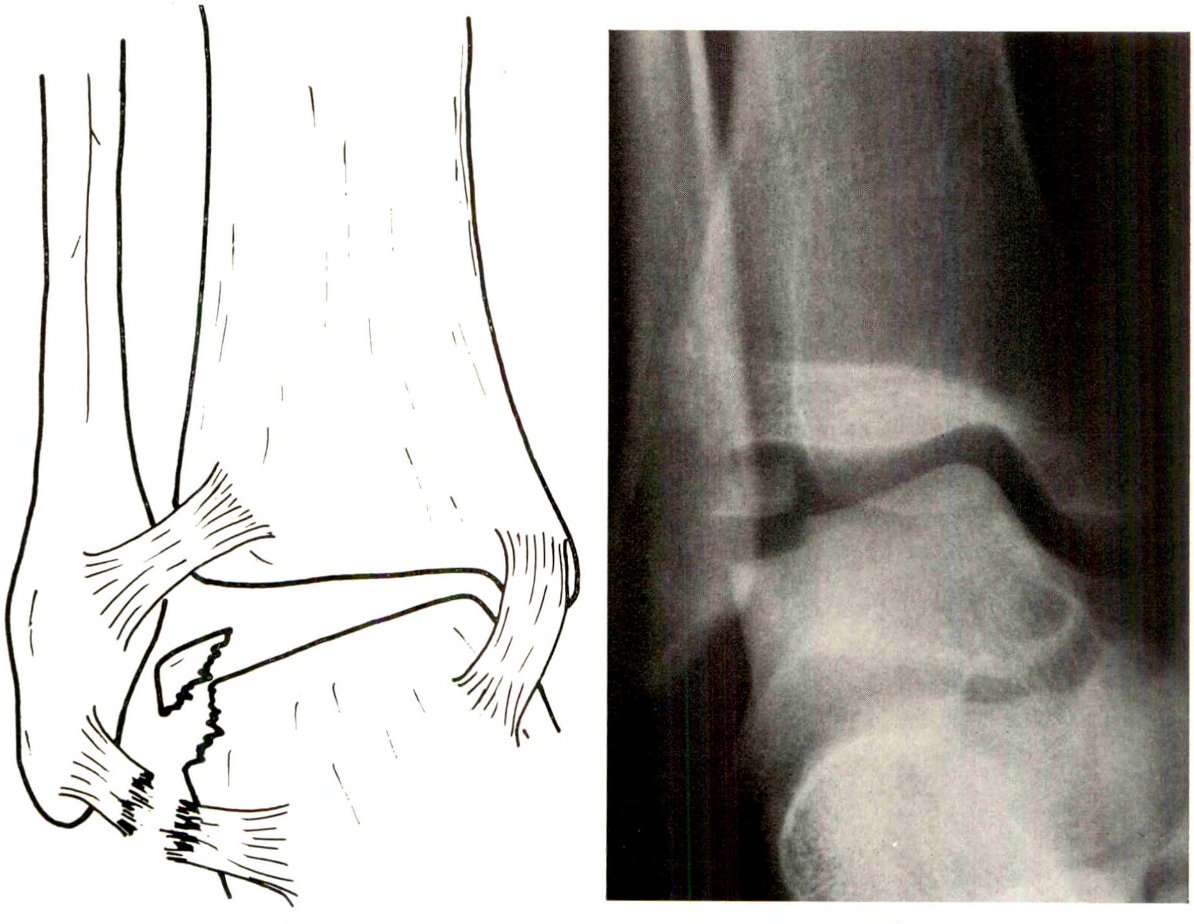


FIG. 1.

(A) Schematic representation of an osteochondral fracture. Inversion with lateral ligament tear causes the lateral dome of the talus to strike the lateral malleolus.

(B) Operative "stress" radiograph demonstrating a fracture which has flipped 180 deg in its bed. There is associated tear of the lateral ligaments.

The fracture may be subtle, and proper radiographic evaluation is essential for accurate diagnosis. Delay in identifying the lesion results in chronic pain, disability and possible irreparable damage to the tibiotalar joint. A need for radiologic awareness of this lesion prompts this report.

Mechanism

It has been shown experimentally (Berndt and Harty, 1959) that lateral dome fractures occur with inversion of the dorsiflexed ankle (Fig. 1). The fracture is located at the middle, or anterior half, of the lateral border of the talus, because in dorsiflexion the wider anterior half of the talus fits snugly into the mortise. Inversion then impacts the lateral dome against the articular surface of the fibula. This injury is usually accompanied by tears of the lateral ligaments.

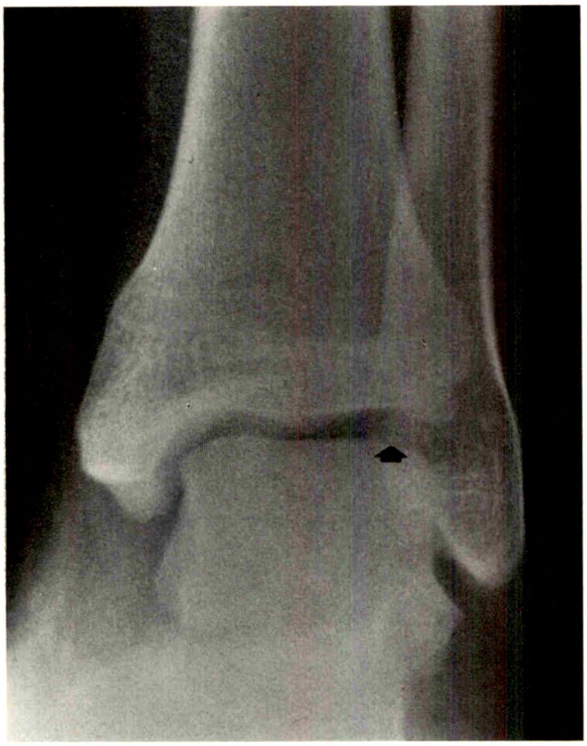
Materials and Methods

In the past three years (June 1974–June 1977) at the Massachusetts General Hospital, 12 surgically proven cases of osteochondral fracture of the talar dome were seen (Table I). Case histories and radiographs were reviewed. There were 11 male patients and one female patient ranging in age from 19 to 53 years, averaging 27 years. Nine patients had lateral dome fractures, two medial. One patient had simultaneous involvement of the medial and lateral dome.

TABLE I

Summary of 12 patients with osteochondral fracture of the talus

Patient	Age, sex	Injury	Ankle	Duration of symptoms	Radiographic findings	Tomograms	Treatment
1	19M	Inversion—tennis	R	6 months pain	Lateral dome	Yes	Arthrotomy—6 × 4 × 2 mm fragment
2	25M	Inversion	L	3 months pain	Lateral dome	Yes	Arthroscopy—fragment removed
3	31M	Inversion	R	2 months pain	Routine films negative	Lat. dome defect seen	Arthrotomy—10 × 8 mm fragment
4	23M	Inversion—basketball	R	1 year pain	Lateral dome	No	Arthrotomy—fragment removed
5	33M	Inversion—jumped from fence	R	4 years pain, swelling	Medial dome	No	Arthrotomy
6	23F	Professional dancer, no hx trauma	L	9 months, locking, popping	Medial and lateral dome	No	Arthrotomy—curette and shave
7	19M	Jumped from freight car	R	6 months pain, swelling and stiffness	Lateral dome	No	Arthrotomy
8	25M	Fall	L	10 days pain	Lateral dome	Yes	Arthrotomy—fragment removed
9	53M	"Twisted ankle"	R	6 months pain and swelling	Medial dome	No	Arthrotomy—fragment removed; deltoid ligament repair
10	19M	Jumped 15ft from balcony	R	2 years pain	Lateral dome	Yes	Arthrodesis for traumatic arthritis—loose bodies removed
11	38M	Inversion—football	R	1 day	Lateral dome fragment flipped 180 deg.	Yes	Arthrotomy—fragment removed
12	20M	Jumped from fence	R	1 hour	Lateral dome fragment flipped 180 deg.	No	Arthrotomy—fragment removed: 15 × 5 mm lateral ligament repair



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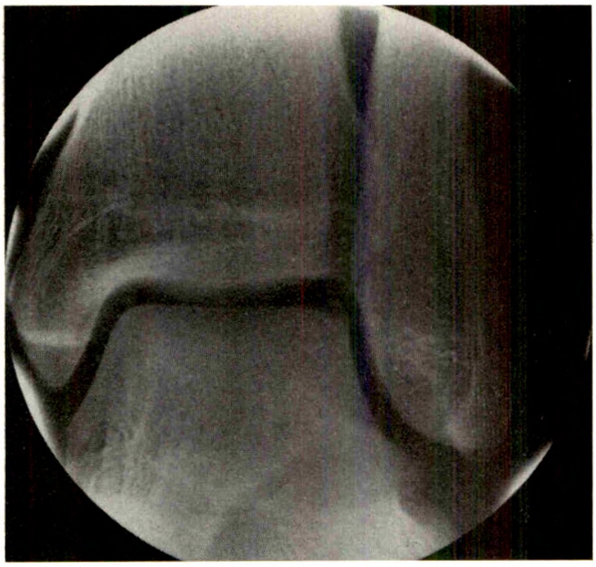

B

Fig. 2

(A) A.P. radiograph demonstrating an osteochondral fracture of the lateral dome of the talus (arrow) which is hidden by the the talus and fibula.

(B) Mortise view of same ankle clearly demonstrating the fracture fragment free of overlap. An associated lucency in the talar dome can be readily identified.

Results

The most striking clinical finding was the duration of symptoms. Most patients were able to describe the offending injury but symptoms persisted for an average of nine months before the accurate diagnosis was established (range two months to 48 months). In four of the twelve patients the radiographic findings were overlooked. Tomography was performed in six cases. One patient had routine ankle radiographs (A.P. lateral and internal oblique) interpreted as normal on three occasions but subsequently tomography revealed an osteochondral fracture of the lateral dome of the talus. Six patients sustained inversion injuries, four jumped from a height, one patient gave a history of a "fall" and one patient had no known history of trauma.

Radiographic Characteristics

Proper radiographic managment of these lesions is essential. A.P. and lateral radiographs of the ankle are not adequate for diagnosis (Roden *et al.*, 1954). The 10 deg internal oblique (mortise view) is mandatory in all ankle trauma. The A.P. view obscures the lateral dome of the talus due to the lateral malleolus overlapping the talus and tibia. The mortise view enables one to view the lateral dome free of overlap because the medial and lateral malleolus are parallel and the talofibular joint is open. This view enables one to see the small flake of bone or crescent shaped defect (Fig. 2). If the fracture is small, however, it still may not be seen. In these circumstances, internal oblique radiographs of the ankle in neutral, plantar flexion and dorsiflexion have been recommended (Yvars, 1976). However, if clinical suspicion is high, tomography is essential. Pluri-directional tomography, in lateral and mortise planes, has been of most value in localizing the fracture fragment. A.P. tomograms may obscure a small fragment due to overlapping shadows. The radiographic size of the fragment is smaller than that seen at operation, because the chondral component is radiolucent. Patient No. 3 had negative radiographs and positive tomography (Fig. 3).

Discussion

Talar dome defects have been described by confusing terminology. Lesions with identical characteristics have been called fractures by some and osteochondritis by others (Berndt and Harty, 1959). Part of the confusion dates back to 1888 when Konig stated that the abnormality was caused by a disease process of unknown origin which he termed osteochondritis dissecans (Campbell and Ranawat, 1966).

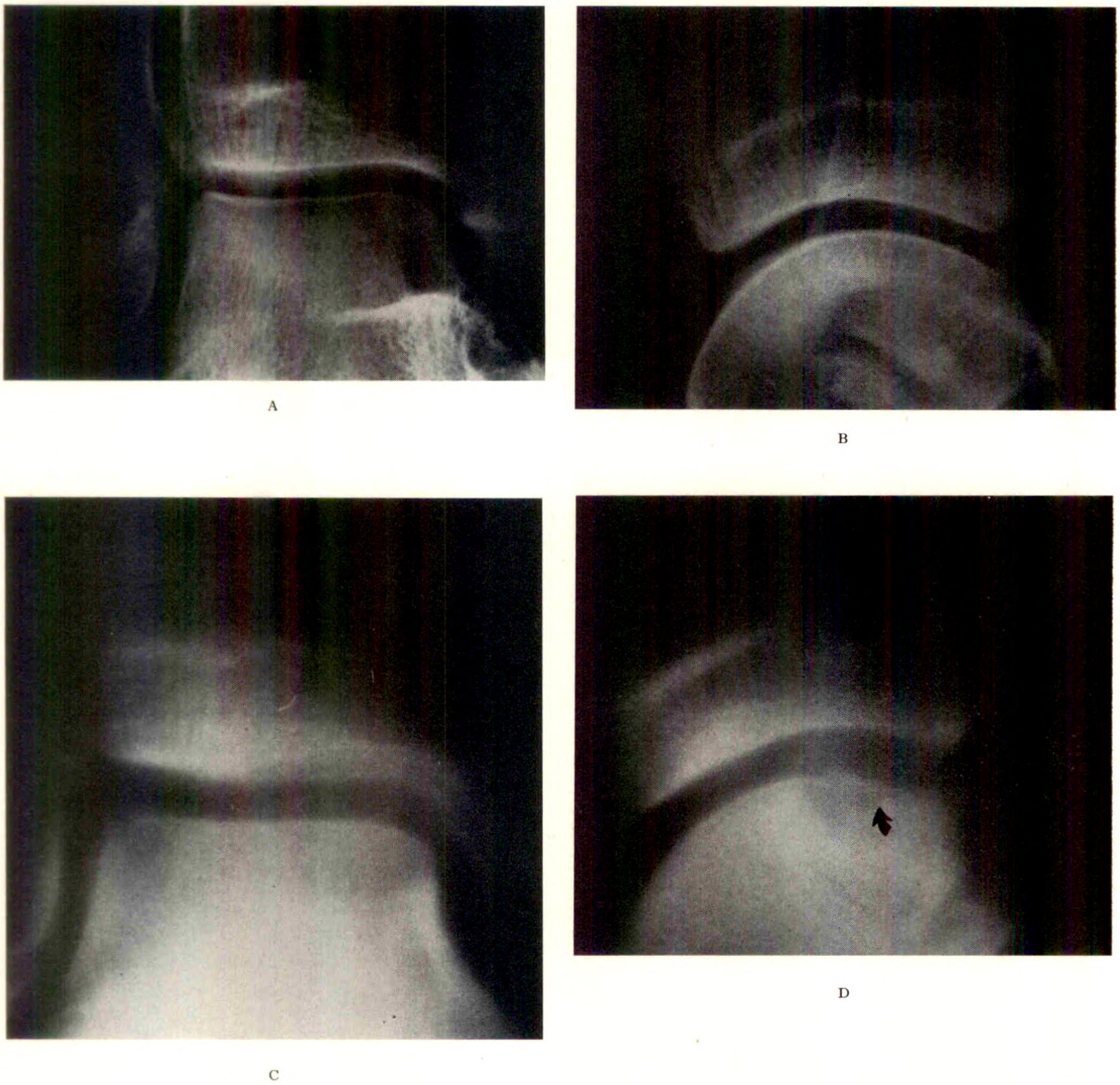

FIG. 3.
(A) Mortise and (B) lateral radiographs were interpreted as normal on several occasions. (C) Internal oblique and (D) lateral tomograms demonstrate a subchondral fracture (arrow) with associated lucency in the talus. At surgery, a loose fragment was removed.

Unfortunately this terminology has persisted in the literature. Although occasionally disputed (Campbell and Ranawat, 1966) it has been shown experimentally that the lesion radiologists recognize as osteochondritis dissecans of the talus is not due to idiopathic avascular necrosis but to injury (Berndt and Harty, 1959; O'Donoghue, 1966).

The medial talar dome is the characteristic location for lesions that the radiologist recognizes as osteochondritis dissecans (Ray and Coughlin, 1947; Vaughan and Stapleton, 1947). Although a history of trauma is frequently lacking, this lesion is the result of a compression injury. Impaction causes damage to the blood supply of the affected segment with resulting necrosis (Berndt and Harty 1959). Many of these patients can be managed conservately because there is no loose joint fragment. It is not intended to discuss this entity further and therefore all cases of medial dome lesions, with the characteristic button of bone surrounded by a lucent rim

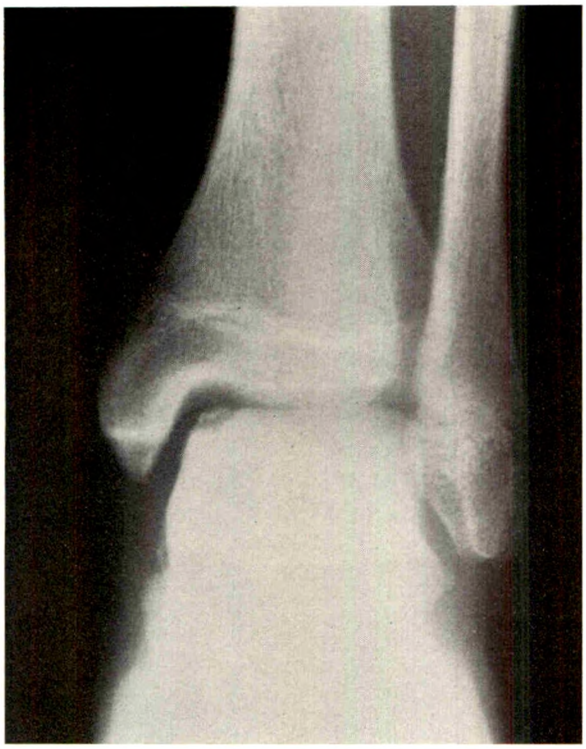

FIG. 4.

Typical radiographic appearance of the lesion radiologists recognize as "osteochondritis dissecans". There is a "button" of bone with surrounding lucent rim.

(Vaughan and Stapleton, 1947), were excluded from this study (Fig. 4).

The most important factor in the recognition of osteochondral fractures of the dome of the talus is an awareness of the condition on the part of the clinician and radiologist (Smith *et al.*, 1977). The possibility should be considered in every ankle injury, especially those with an inversional component (Mukherjee and Young, 1973; Smith *et al.*, 1977). After an acute inversion injury, lateral ligament injury may initially overshadow the osteochondral fracture.

After the acute injury, there is a latent period during which disability is slight and the diagnosis may be overlooked. Soon however, a chronic period will ensue. Patients with persistent pain, especially between the talus and tibiofibular syndesmosis, should be suspect. Tenderness, crepitation, recurrent swelling, clicking or symptoms of a 'weak ankle' all raise the possibility of a fracture of the dome of the talus (DeGrinder, 1955; Yvars, 1976). Chondral or osteochondral injury should be suspected if the clinical symptoms seem out of proportion to the findings. Tomography is strongly recommended in suspected osteochondral fracture of the talar dome even with negative routine ankle radiographs (Blom and Strijk, 1975; Ray and Coughlin, 1947).

Some of these lesions can be managed conservatively but most authors feel that surgical removal of the loose fragment and repair of ligamentous damage offers better results (Berndt and Harty, 1959; Blom and Strijk, 1955). Delay in surgical removal of a loose fragment may result in post-traumatic arthritis and possible arthrodesis (Davidson *et al.*, 1967).

REFERENCES

BERNDT, A. L., and HARTY, M., 1959. Transchondral fractures (osteochondritis dissecans) of the talus. *Journal of Bone and Joint Surgery 41A*, 988–1020.

BLOM, J. M., and STRIJK, S. P., 1975. Lesions of the trochlea tali. Ostoechondral fractures and osteochondritis dissecans of the trochlea tali. *Radiologia Clinica (Basel)*, *44*, 387–396.

CAMPBELL, C. J. and RANAWAT, C. S., 1966. Osteochondritis dissecans: the question of etiology. *Journal of Trauma*, *6*, 201–221.

COLTART, W. D., 1952. Aviator's astragalus. *Journal of Bone and Joint Surgery*, *34B*, 545–566.

DAVIDSON, A. M., STEELE, H. D., MACKENZIE, D. A., and PENNY, J. A., 1967. A review of 21 cases of transchondral fracture of the talus. *Journal of Trauma*, 7, 378–415.

DEGINDER, W. L., 1955. Osteochondritis dissecans of the talus. *Radiology*, *65*, 590–598.

MUKHERJEE, S. K., and YOÜNG, A. B., 1973. Dome fracture of the talus. A report of 10 cases. *Journal of Bone and Joint Surgery*, *55B*, 319–326.

NISBET, N. W., 1954. Dome fracture of the talus. *Journal of Bone and Joint Surgery*, *36B*, 244–246.

O'DONOGHUE, D. H., 1966. Chondral and osteochondral fractures. *Journal of Trauma*, *6*, 469–481.

RAY, R. B., and COUGHLIN, E. J., 1947. Osteochondritis dissecans of the talus. *Journal of Bone and Joint Surgery*, *29*, 697–706.

RODEN, S., TILLEGARD, P., and UNANDER-SCHARIN, L., 1954. Osteochondritis dissecans and similar lesions of the talus. *Acta Orthopaedica Scandinavica*, *23*, 51–66.

SMITH, G. R., WINQUIST, R. A., ALLAN, T. N., and NORTHROP, C. H., 1977. Subtle transchondral fractures of the talar dome: a radiological perspective. *Radiology*, *124*, 667–673.

VAUGHAN, C. E., and STAPLETON, J. G., 1947. Osteochondritis dissecans of the ankle. *Radiology*, *49*, 72–78.

YVARS, M. F., 1976. Osteochondral fractures of the dome of the talus. *Clinical Orthopaedics and Related Research*, *114*, 185–191.

1979, *British Journal of Radiology*, *52*, 110–115

Lymphography in angio-immunoblastic lymphadenopathy

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ABSTRACT

Angio-immunoblastic lymphadenopathy (AIL) produces a characteristic lymphoproliferative syndrome, with characteristic lymphographic appearances. The authors studied the lymphographic manifestations of 18 cases of AIL. In 15 out of 18 cases, enlargement is observed in all the lymph nodes with a lacy or reticular storage pattern and sharp, well delimited margins. This lymphographic appearance reflects the histologic changes; only the peripheral sinuses, which are not involved, can be observed on lymphography.

A recently recognized entity, angio-immunoblastic lymphadenopathy (AIL) is a specific lymphoproliferative syndrome. Since the first publications (Frizzera *et al.*, 1974; Horne *et al.*, 1974; Lukes and Collins, 1974; Nomanbhoy and Prager, 1974; Tangun *et al.*, 1974), the main reports have been published by the teams of Rappaport, Lennert and Flandrin (Frizzera *et al.*, 1975; Radaszkiewicz and Lennert, 1975; Flandrin, 1976).

The diagnosis is based on histologic findings of a lymph node biopsy: (1) hypervascularization which predominates in the paracortical region; (2) a lymphoplasmo-immunoblastic reaction; (3) P.A.S. interstitial deposits, especially in the cortical and para-cortical regions. According to Radaszkiewicz and Lennert (1975) these deposits are inconstant. Sometimes epithelioid histiocytes prevail and these three histologic criteria may be masked (Frizzera *et al.*, 1975). A particular characteristic of AIL is the fact that the peripheral sinus does not become involved.

More than 200 cases have been reported and AIL's radiological particularities have been emphasized by Libschitz *et al.* (1977); Serres *et al.* (1977), and Zylak *et al.* (1976).

Although 42 lymphograms have been performed in these series, it is our view that insufficient attention has been paid to the findings. The aim of the present study is to document the lymphographic changes in 18 cases of AIL and to compare these with the described histology.

PATIENTS and METHODS

From 1968 to 1977 18 patients with AIL were seen at the "Fondation Bergonié", Bordeaux, France. Lymph node biopsies were systematically performed; for nine cases the diagnosis of AIL was established retrospectively during a review of the slides of a series of malignant lymphomas (Meugé and Mascarel, 1977).

The ages ranged from 24–84 years with a mean age of 62 years. There were 13 males and five females. Most of the patients in our series presented a similar clinical picture. Generally speaking, they were elderly patients presenting with generalized disease and fever (16 cases), weight loss (14 cases), sweating (12 cases), asthenia (12 cases), accompanied

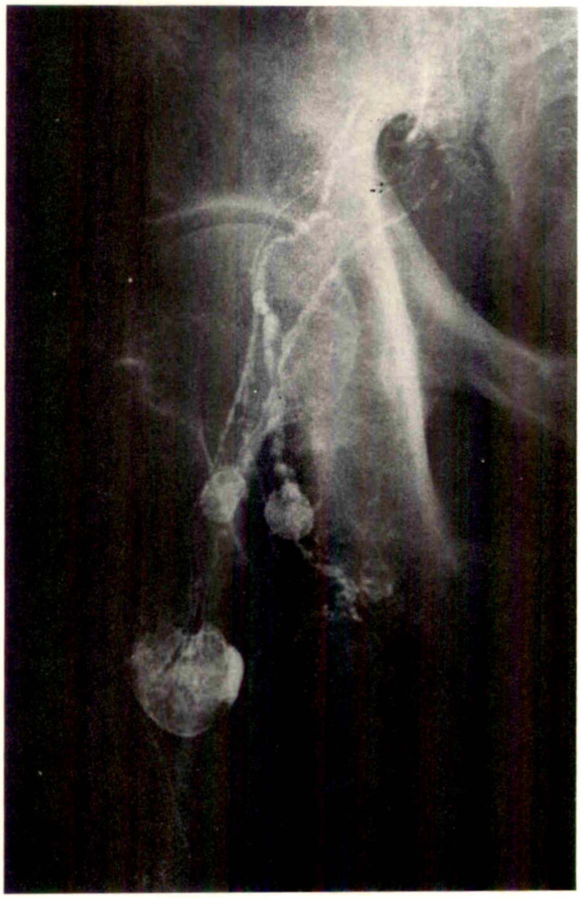

FIG. 1.

AIL, typical appearance on the lymphangiogram: close-up view of enlarged inguinal nodes with a lacy and reticular storage pattern. Sharp well delimited margins. Normal lymph vessels.

TABLE I

Age and sex	Topography	Morphology
58 F	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins
71 F	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins
67 F	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins
42 M	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins; a few zones with granular pattern
51 M	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins; a few zones without apparent margins; a few zones with granular pattern
63 M	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins; a few zones without apparent margins
70 M	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins; a few zones with granular pattern
53 M	Localized lumbar enlargement	Lacy or reticular pattern; a few defects
65 M	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins; a few zones with defects
28 M	Localized iliac enlargement	Granular pattern
61 F	Diffuse enlargement; predominating in the iliac region	Granular pattern
52 M	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins
62 M	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins; a few zones without apparent margins
84 M	Diffuse enlargement; predominating in the iliac region	Lacy or reticular pattern; sharp and well delimited margins; a few zones without apparent margins
56 F	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins
74 M	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins; persistance of opacification of lymph vessels on the lymphogram
41 M	Localized left iliac enlargement	Lacy or reticular pattern; sharp and well delimited margins
65 M	Diffuse enlargement	Lacy or reticular pattern; sharp and well delimited margins; a few zones with granular pattern

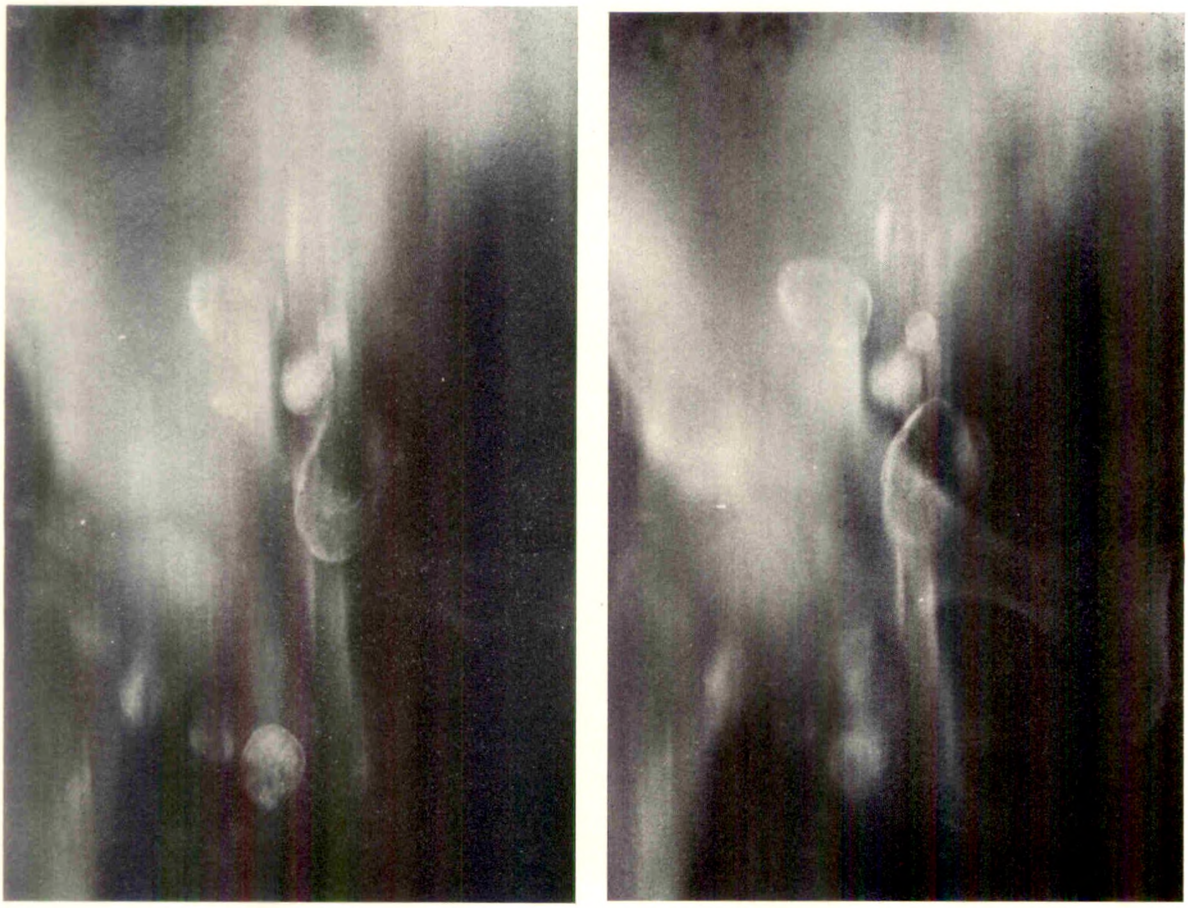

FIG. 2.

Tomograms of typical enlarged inguinal nodes: the reticular pattern is due to visualization of the peripheral sinus whereas the central part of the lymph node is only slightly opacified.

by skin minifestations such as pruritis (17 cases) or skin rash (14 cases). Superficial lymphadenopathy was almost always generalized (17 cases); it was localized in only one case. Splenomegaly was present in 11 cases and hepatomegaly in nine. Biologic disorders encountered were: hyperimmunoglobulinaemia (16 cases), haemolytic anaemia with positive Coomb's test (15 cases) and increased erythrocyte sedimentation rate (15 cases).

Neither diagnostic laparotomy nor splenectomy were undertaken. Three autopsies were performed.

In all cases, bilateral lymphography was performed within the first three months of the affection. In three cases tomograms of involved nodes were also performed.

RESULTS

The lymphograms were never normal. The frequency of lymphographic abnormalities is noted in Table I.

The positions of the lesions were: diffuse with homogeneous enlargement of lymph nodes in all regions (seven cases); diffuse enlargement but predominating in the iliac region (eight cases); localized with atypical enlargement (iliac: one case; lumbo-aortic: one case) and a normal appearance in other regions; localized and typical enlargement with moderate hyperplasia in other regions (one case).

Morphologically, the following lymphographic manifestations may be associated: lacy or reticular pattern of the lymph nodes (16 cases), lacy or reticular pattern with sharp and well-delimited margins (typical appearance) (15 cases), (Figs. 1 and 2), granular pattern of the lymph nodes (five cases), (Fig. 3), lacy or reticular pattern and a few zones without apparent margins (five cases) (Fig. 4),

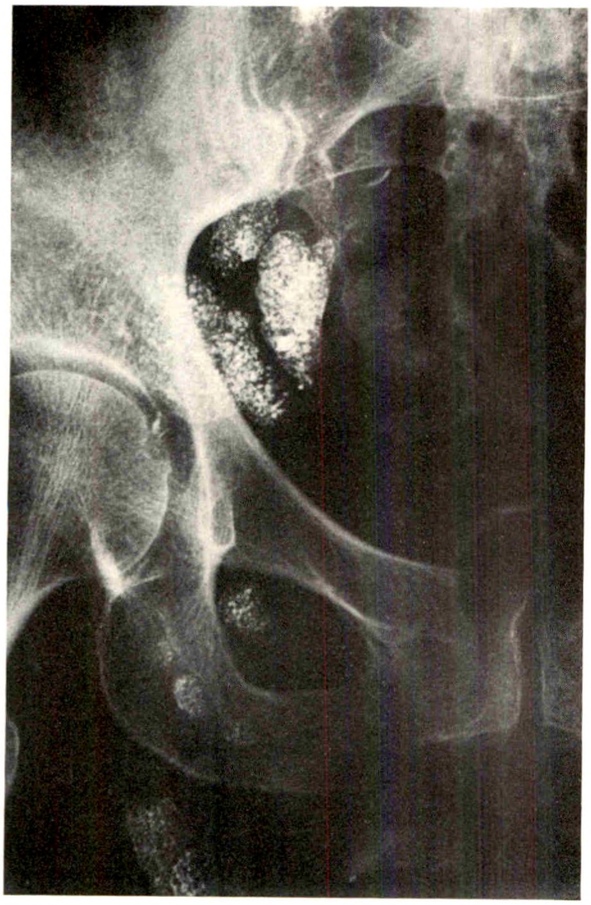

FIG. 3.

AIL appearance on lymphadenogram: close-up view of slightly enlarged iliac nodes with granular pattern. No defect.

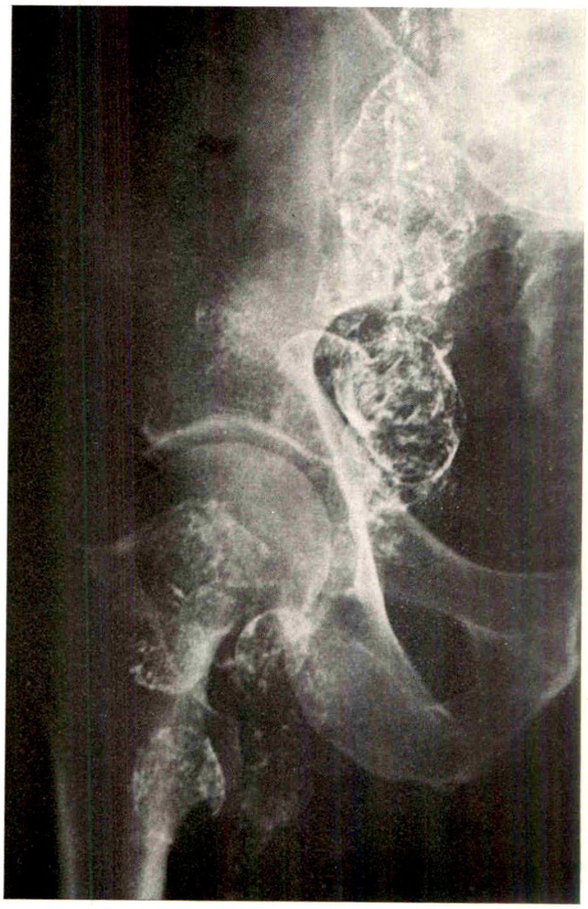

FIG. 4.

AIL appearance on lymphadenogram: close-up of the iliac nodes with enlargement and reticular storage pattern of lymph nodes. Some non-opacified margins.

localized defects (two cases) (Fig. 5), persistence of opacification of the lymph vessels on the lymphogram (one case).

The lymph nodes were not extremely large in any of the cases: the transverse diameter, measured on a P.A. view, never exceeded 2.5 cm, taking into account an average magnification of 1.2.

Tomograms performed in three cases had a typical appearance; they showed lacy and reticular patterns in the peripheral sinus.

DISCUSSION

The different frequencies involving age, sex and clinical symptoms noted in our observations are similar to those mentioned in other series (Frizzera *et al.*, 1975; Radaszkiewicz and Lennert, 1975; Flandrin, 1976).

Only 42 of the patients previously published underwent lymphography. This examination is useful in establishing the diagnosis of AIL, as the appearance of the lymphogram is often typical (Mathe *et al.*, 1976; Rochant *et al.*, 1976; Libschitz *et al.*, 1977; Rouanet *et al.*, 1977; Serres *et al.*, 1977).

In fact, these appearances are explained by the histologic lesions. In AIL the normal morphologic structure of the lymph node disappears and is replaced by vascular and cellular proliferation. In all cases the capsule is infiltrated; sometimes the involvement extends beyond the capsule, but the peripheral sinuses do not become involved; this factor aids in ruling out the diagnosis of malignant lymphoma (Figs. 6 and 7).

The lesions are generally widespread, predominating in the iliac regions. Rouanet *et al.* (1977) and Serres *et al.* (1977), state that all the lymph nodes of a given chain are abnormal, but, on the other hand

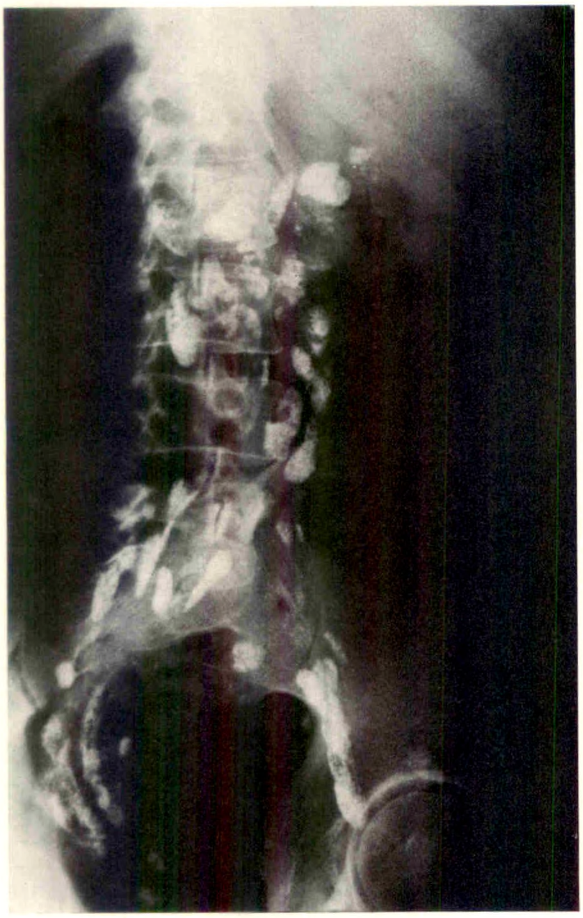

FIG. 5.

AIL appearance on lymphadenogram: lumbar node involvement with extensive defects. Small defects in the lumbar lymph nodes.

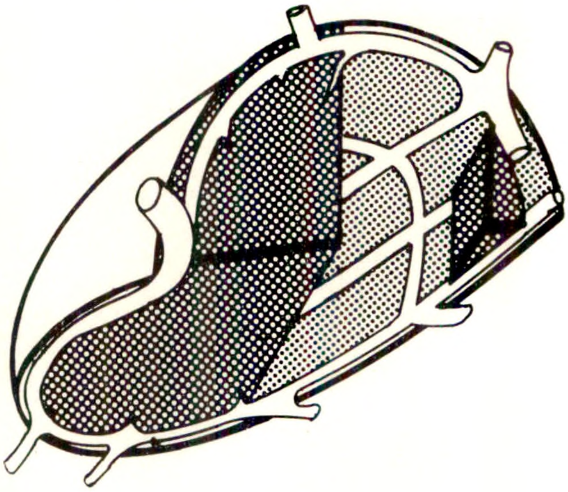

FIG. 6.

Diagram of a normal lymph node in which the canals have been enlarged for demonstration purposes.

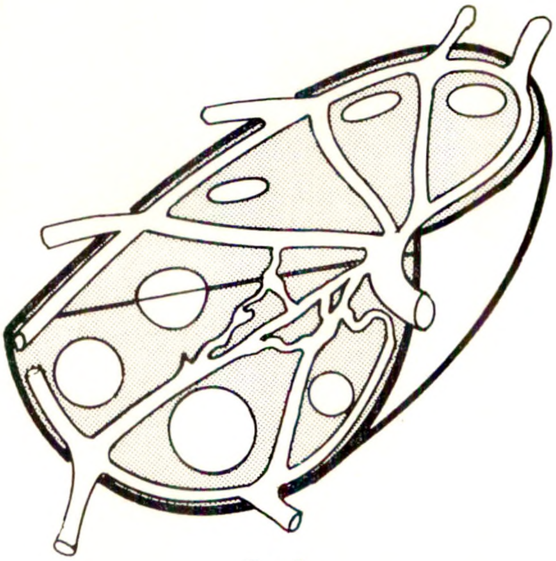

FIG. 7.

Diagram of AIL's lymph node: the central part of the lymph node, the radial sinuses are involved. The peripheral sinuses are not involved, thus explaining the lacy or reticular pattern with well delimited margins.

Thomas *et al.* (1976) describe, as we do, one case with an isolated lesion. The lacy or reticular pattern is described by all authors. The granular pattern is less frequently observed (Serres *et al.*, 1977). Characteristically, the lymph node margins in AIL are sharply defined. Thus the image most frequently observed is a lacy or reticular pattern with sharp and well-delimited margins.

However, this appearance is not found in every case (Thomas *et al.*, 1976). It depends on visualization of the peripheral sinus, whereas the central part of the lymph node is only slightly, or not at all opacified. On tomograms this opacification is linear and irregular, thus explaining the invisibility of the margin in some lymph nodes. The association of these lymphographic signs seems to differentiate AIL from Hodgkin's disease. In Hodgkin's disease some lymph nodes have a normal appearance, whereas other nodes in the same chain show filling defects (Lamarque *et al.*, 1967).

In non-Hodgkin lymphomas only a few groups of lymph nodes may be involved; there is a very marked enlargement; the peripheral sinuses are involved, and thus the typical appearance encountered in AIL is not found here. In chronic lymphatic leukaemia all the lymph node chains are involved. The lymph nodes are enlarged and have a granular appearance. Tuberculosis is characterized by moderately enlarged lymph nodes with irregular and patchy defects (Betoulieres *et al.*, 1968). Collagen diseases are characterized by lymph nodes which are moderately hypertrophied with regular and granular patterns. These lymphographic results differ, in most cases, from those of AIL (Rauste, 1972; Lagarde *et al.*, 1975).

Even though the diagnostic value of lymphography is more topographic than aetiologic, the typical appearance of the AIL view should be emphasized. Finally, in most cases, the lymphographic appearance reflects the histologic pattern; thus only the peripheral sinuses, which are not involved, can still be observed on lymphography. This feature results in lymphographic findings which are often characteristic of the disease.

REFERENCES

BETOULIERES, P., LAMARQUE, J. L., GINESTIE, J. F., and COMBES, C., 1968. Etude des aspects lymphographiques de la tuberculose ganglionnaire. *Journal de Radiologie d'Electrologie et de Médicine Nucléaire*, *49*, 1–6.

FLANDRIN, G., 1976. Adénopathies angio-immunoblastiques avec anémie auto-immune et hyperimmunoglobulinémie polyconale. *Nouvelle Presse Médical*, *5*, 1521–1524.

FRIZZERA, G., MORAN, E. M., and RAPPAPORT, H., 1974. Angio-immunoblastic lymphadenopathy with dysproteinaemia. *Lancet*, *1*, 1070–1073.

1975. Angio-immunoblastic lymphadenopathy. Diagnosis and clinical course. *American Journal of Medicine*, *59*, 803–818.

HORNE, C. H. W., FRASER, R. A., and PETRIE, J. C., 1974. Angio-immunoblastic lymphadenopathy with dysproteinaemia. *Lancet*, *2*, 291.

LAGARDE, C., CHAUVERGNE, J., and HOERNI, B., 1975. In *Les lymphomes malins*, pp. 41–42. (Ed. Masson, Paris).

LAMARQUE, J. L., PAGES, A., PUJOL, H., GINESTIE, J. F., and COMBES, C., 1967. Anatomie radiologique et valeur séméiologique des images ganglionnaires en lymphographie. *Journal de Radiologie d'Electrologie et de Médicine Nucléaire*, *48*, 253–262.

LIBSHITZ, H. I., CLOUSER, M., ZORZONA, J., and OSBORNE, B. M., 1977. Radiographic findings of immunoblastic lymphadenopathy and related immunoblastic proliferative. *American Journal of Roentgenology*, *129*, 875–878.

LUKES, R. J., and COLLINS, R. D., 1974. Immunologic characterization of human malignant lymphomes. *Cancer*, *34*, 1488–1503.

MATHÉ, G., AMIEL, J. L., MACHOVER, D., GERARD-MARCHANT, R., and CAILLOU, B., 1976. La lymphadénite angio-immunoblastique. *Annales de Médecine Interne (Paris)*, *127*, 849–856

MEUGÉ, C., and MASCAREL, A. DE, 1977. Lymphadénopathie angio-immunoblastique. *Archives d'Anatomie et de Cytologie Pathologique*, *25*, 187–189.

NOMANBHOY, Y. T. and PRAGER, P. R., 1974. Angio-immunoblastic lymphadenopathy with dysproteinaemia. *Lancet*, *2*, 409.

RADASZKIEWICZ, T. and LENNERT, K., 1975. Lymphogranulomatosis X. *Deutsche Medizinisch Wochenschrift*, *100*, 1157–1163.

RAUSTE, J., 1972. Lymphographic findings in granulomatous inflammations and connective tissue diseases. Differential diagnosis between these diseases and lymphomas. *Acta Radiologica Supplementum 317*, 80.

ROCHANT, H., REYES, F., VERNANT, J. P., BRUN, B., SCHAEFFER, A., SULTAN, C., TULLIEZ, M., LEBEZU, M., and DREYFUS, B., 1976. Aspects évolutifs de la lymphadénopathie angio-immunoblastique. A propos de 3 observations. *Annales de Radiologie*, *20*, 179–184.

ROUANET, J. P., DUPERRAY, B., FRIQUET, M., TABOURY, J., and GORIN, C., 1977. La lymphadénopathie angio-immunoblastique. Aspects lymphographiques. A propos de deux observations. *Annales de Radiologie*, *20*, 179–184.

SERRES, J. J., BUTORI, P. J., COUSSEMENT, A., and CASSUTO, G. P., 1977. Aspects lymphographiques de la lymphadénopathie angio-immunoblastique. *Journal de Radiologie d'Electrologie et de Médecine Nucléare*, *58*, 641–645.

TAGUN, Y., SARACBASI, Z., PEKCELEN, Y., and INCEMAN, S., 1974. Angio-immunoblastic lymphadenopathy with dysproteinaemia. *Lancet*, *1*, 1345–1346.

THOMAS, M., MANDARD, J. C., TANGUY, A., PONCEY, C., BENARD, Y., and LEMENAGER, J., 1976. Manifestations respiratoires de la lymphadénopathie angio-immunoblastique. A propos de quatre cas. *Revue Française des Maladies Respiratoires*, *4*, 577–588.

ZYLAK, C. J., BANERJEE, R., GALBRAITH, P. A., and MACCARTHY, D. S., 1976. Lung involvement in angio-immunoblastic lymphadenopathy (AIL). *Radiology*, 121, 513–519.

1979, *British Journal of Radiology*, *52*, 116–123

Clinical evaluation of computer processing of liver gamma camera scans

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ABSTRACT

A prospective study to assess the clinical usefulness of computer processing of liver scans has been carried out on 203 patients. All patients have had six months follow up to confirm the diagnostic accuracy of the scan results. Four presentations have been studied using ROC analysis:

(i) original gamma-camera pictures;
(ii) processed images obtained using a non-stationary filter;
(iii) images processed using nine-point smoothing;
(iv) images obtained by linear interpolation at 25 isocount levels of display.

It is concluded that pictures obtained by use of a non-stationary filter at 25 isocount levels are superior to conventional gamma-camera pictures and displays obtained by linear interpolation only. All three are considerably superior to the images obtained by nine-point smoothing in detection of focal space-occupying lesions. Based on the results obtained, a strategy for the rational use of computer processing of gamma-camera liver scans is proposed.

In static imaging computers have been used to reduce statistical noise and to enhance contrast. The results obtained so far are conflicting. The conclusions drawn vary from "computer displays are superior" (Tauxe, 1968; Gustafsson and Pizer, 1975) to "computer displays produce no change in index of detectability" (Kuhl *et al.*, 1972) to "computer produces increase in false positive rate" (Sebern *et al.*, 1976). We started this project primarily to resolve this confusion. In the first part of the project the value of various isocount levels in determining the sensitivity of liver scanning in detecting focal lesions was assessed, and in the second part the processing of these isocount levels was assessed. The results of the first part of the study, which have been reported fully (Rai, 1977; Rai *et al.*, 1977), show that in isocount display 25 levels is the best number of isocount levels at which to see a smoothed image of the liver and that this is better than the original gamma-camera scan. In the second part the effect of nine point smoothing and processing by a non-stationary filter developed by Alpert *et al.* (1977) on this isocount level was assessed. The results of this study are presented here.

METHOD

All liver scans were carried out on a gamma camera (Ohio-Nuclear 100 series) linked to a Nova-2 computer. Each patient was given 1 mCi of $^{99}\text{Tc}^{\text{m}}$ labelled sulphur colloid and four views were recorded using a diverging collimator, *i.e.* anterior, anterior with lead marker to outline the costal margin, posterior and right lateral. The number of counts collected was 100 k for anterior and posterior views, and 80 k for the lateral view. The data of each view (*i.e.* X and Y pulses) from the gamma camera were stored on 64×64 matrix. The data were then transferred onto a magnetic disk for storage. At the end of each day all scans were displayed in three different ways: by using linear interpolation from 64^2 to 128^2 at isocount level 25 (without smoothing or enhancement); by using nine-point smoothing; and by using a non-stationary filter developed by Alpert *et al.* (1977). The filter used had two parameters h and s. The parameter h determined the shape of the filter near zero frequency and thus can be said to represent the degree of enhancement; and the parameter s determined the minimum signal-to-noise ratio required in the final image and thus can be said to represent the degree of smoothing. The actual mathematical relationship of these parameters, as modified by J. D. Fenwick at Newcastle General Hospital, Newcastle upon Tyne, can be summarized as follows:

The shape of the filter in the spatial domain is defined by:

$$\begin{aligned} f(x) &= a_1 \text{ for } -L_{1/2} \leq x \leq L_{1/2} \\ &= a_2 \text{ for } -L_{2/2} \leq x < -L_{1/2} \\ &= a_2 \text{ for } L_{1/2} < x \leq L_{2/2} \end{aligned}$$

Where a_1 and a_2 aer gains and L_1 and L_2 are the integers.

The Fourier Transform ($F(W)$) can be written:

$$F(W) \rightarrow 1 + hw^2/24 \text{ as } w \rightarrow 0 \quad \ldots\ldots\ldots\ldots(1)$$

which leads to the conditions:

$$a_1\, L_1 + a_2\, (L_2 - L_1) = 1 \quad \ldots\ldots\ldots\ldots\ldots\ldots(2)$$

$$a_1\, L_1^3 + a_2\, (L_2^3 - L_1^3) = -h \quad \ldots\ldots\ldots(3)$$

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If L_1 and L_2 are defined by:

$L_1=2n+1$; $L_2=(2n+1+(-1^n))/2$ $n=1, 2\ldots\ldots$
Then equations (2) and (3) can be solved for a_1, h, and a_2 for each value of n.

The algorithm is implemented as follows:
$f(x)$ is generated for $n=1$ and convoluted with the image to give an output N. If the condition

$$N^2=s^2\, a^2(N) \quad \ldots\ldots\ldots\ldots\ldots(4)$$

is satisfied, then N replaces the original data point, otherwise h is increased and the process repeated until equation (4) is satisfied. This is done for each point in the image. The entire process is then repeated with $f(y)$ to give a two-dimensional image. On the initial assessment $n=1$ produced artefacts when s was specified to be less than the signal-to-noise ratio of the image. Therefore the algorithm was started at $n=2$ and terminated at $n=5$.

To assess the filter objectively it was decided that one value of each of the two parameters h and s should be chosen despite the fact that theoretically the smoothing and enhancement required would vary from scan to scan depending on size of lesion, count density, etc. The optimum values of h and s were chosen by looking at ten scans of patients in whom the histological diagnoses were known. These ten scans consisted of five cases who had definite space-occupying lesions, four patients who had normal livers and one patient who had cirrhosis. The anterior view of each scan was processed with varying degrees of smoothing (s) and enhancement (h). The values used for h were 0, 5, 10, 15 and 20 and for s 0, 10, 15, 20 (although the value of s was stated as 0 on command, the actual value was 6–7 because of the signal-to-noise ratio of the images.

All the scans displayed with varying values of h and s were reported blindly by two individuals using confidence grading 0–4 (where 0, 1 and 2 are respectively 100%, 75–90% and 50% certainty of presence of no space-occupying lesions and 3 and 4 are 75–90% and 100% certainty of presence of space-occupying lesions). Two observers reported the scans twice, over one week, so as to provide adequate numbers for plotting ROC (receiver operating characteristics) curves. The scans with the best values of h and s from the curves for the two individuals were then assessed subjectively knowing the diagnoses. From this procedure one value of h with one value of s were picked which displayed the space-occupying lesions most clearly and yet did not produce too many artefacts. This was done to introduce some objectivity although the one level of enhancement and smoothing cannot be optimum for all scans. It is not clear from previous reports how other groups have tried to solve this problem. One can only assume that a value was picked for smoothing or enhancement depending on what they expected to see on the scan. Although this is probably ideal for a nuclear medicine department for a day to day service as suggested by L. J. Quinn III (1972), this cannot be used for a clinical trial where subjective elements should be minimal.

The overall accuracy of processing was assessed both by ROC curves drawn for four observers (three

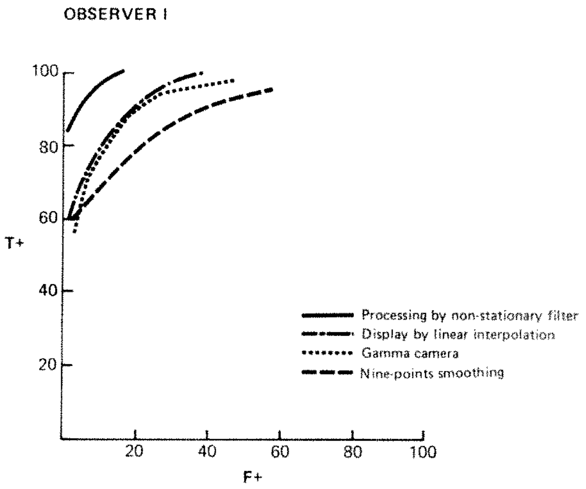


FIG. 1.

ROC curves for observer I constructed (using all scans) for four different modes of presentation of scans, *i.e.* gamma camera scans, scans displayed at 25 isocount levels by linear interpolation, scans processed by non-stationary filter and scans processed by nine-point smoothing. Processing by non-stationary filter is clearly the best.

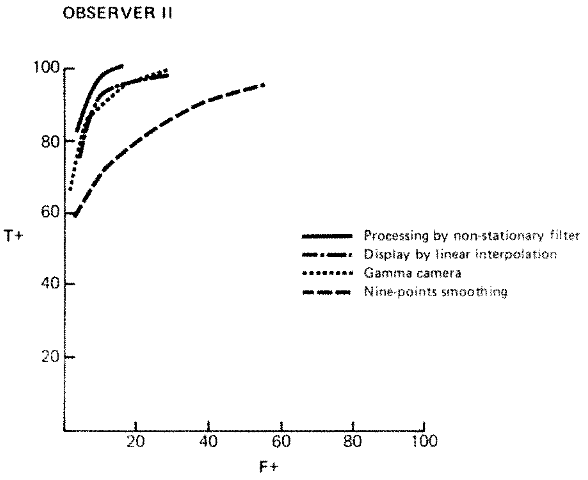


FIG. 2.

ROC curves for observer II constructed in the same way as Fig. 1.

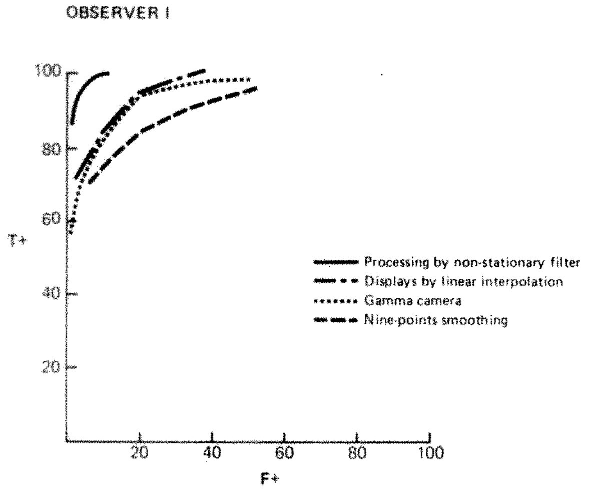


Fig. 3.

ROC curves for observer I constructed using all scans except those of patients who had known chronic liver disease or signs of chronic liver disease at the time of scanning. All the curves are moved towards the left hand corner of the graph by this manoeuvre.

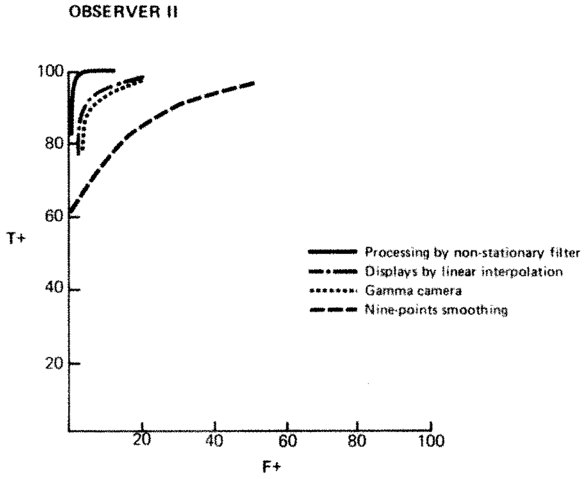


Fig. 4.

ROC curves for observer II constructed in the same way as Fig. 3. The improvement is more obvious on the curve for the non-stationary filter. The curve for the filter reaches a near ideal position with a true positive rate of 100% and a very small false positive rate.

TABLE I

True and false positive and negative rates for four different types of presentation of scans

	True positive fraction	True negative fraction	False positive fraction	False negative fraction
Processed scans (non-stationary filter)	53/53=1	134/150=0.89	16/150=0.11	0
Display by linear interpolation at 25 isocount levels	47/53=0.89	140/150=0.93	10/150=0.07	6/53=0.11
Gamma-camera scans	43/53=0.85	143/150=0.95	7/150=0.05	8/53=0.15
Scans with nine point smoothing	32/53=0.60	143/150=0.95	7/150=0.05	21/53=0.40

TABLE II

Statistical comparison (chi square values) of T positive values of various types of display

	Processed scans (non-stationary filter)	25 isocount levels displays	Gamma-camera scans	Nine point smoothing
Processed scans (non-stationary filter)		4.416*	8.83*	23.75**
25 isocount level displays			0.082 (NS)	9.74**
Gamma-camera scan				6.84**
Nine point smoothing				

*=Significant at 0.05 level of probability.
**=Significant at 0.01 level of probability.
NS=Not significant.

physicians and one physicist), since it is the best way of analysing the results and of forming diagnostic strategies (Metz *et al.*, 1977), and by calculating true positive, false positive, true negative and false negative fractions.

All patients were followed while in hospital and thereafter for six months at regular intervals. Where possible, histological findings, autopsy findings or laparotomy findings were obtained and correlated with clinical diagnoses and scan reports.

RESULTS

Assessment of parameters h *and* s *of the filter*

The ROC curves drawn show that the value of h and s that produced the best results for observer I were $h=10$, $s=0$, and $h=10$ and $s=10$; and for observer II were $h=15$, $s=0$ and $h=15$, $s=10$. Our subjective reporting showed that as smoothing, *i.e.* the value of s, was increased the scan became blurred and the obvious lesions on the gamma camera scan were lost. Correspondingly as the value of h (*i.e.* enhancement) was increased, the noise was brought out even in the normal scan. From this we concluded that a near optimum value of h and s should be somewhere in the middle range, *i.e.* $h=10$–15, and $s=10$–15 as suggested by ROC curves for two observers. From the subjective assessment the values of the parameters picked out for objective assessment were $h=10$, $s=10$. These were the values of the parameters of the non-stationary filter which produced fewest artefacts on the scans reviewed and yet enhanced the lesions present in the gamma-camera scans. These were the values used to process the next 250 scans.

Results of processing using nine-point smoothing and a non-stationary filter

In total 250 scans were displayed by linear interpolations from $64^2 \rightarrow 128^2$, by nine point smoothing, and with the non-stationary filter. Satisfactory clinical follow-up was available on 203 patients only (155 had diagnoses made by needle biopsy, at laparotomy or at autopsy: 33 had normal scans and at six months were clinically well, and 15 patients with obvious multiple space-occupying lesions in the liver and proven primary malignancy elsewhere were

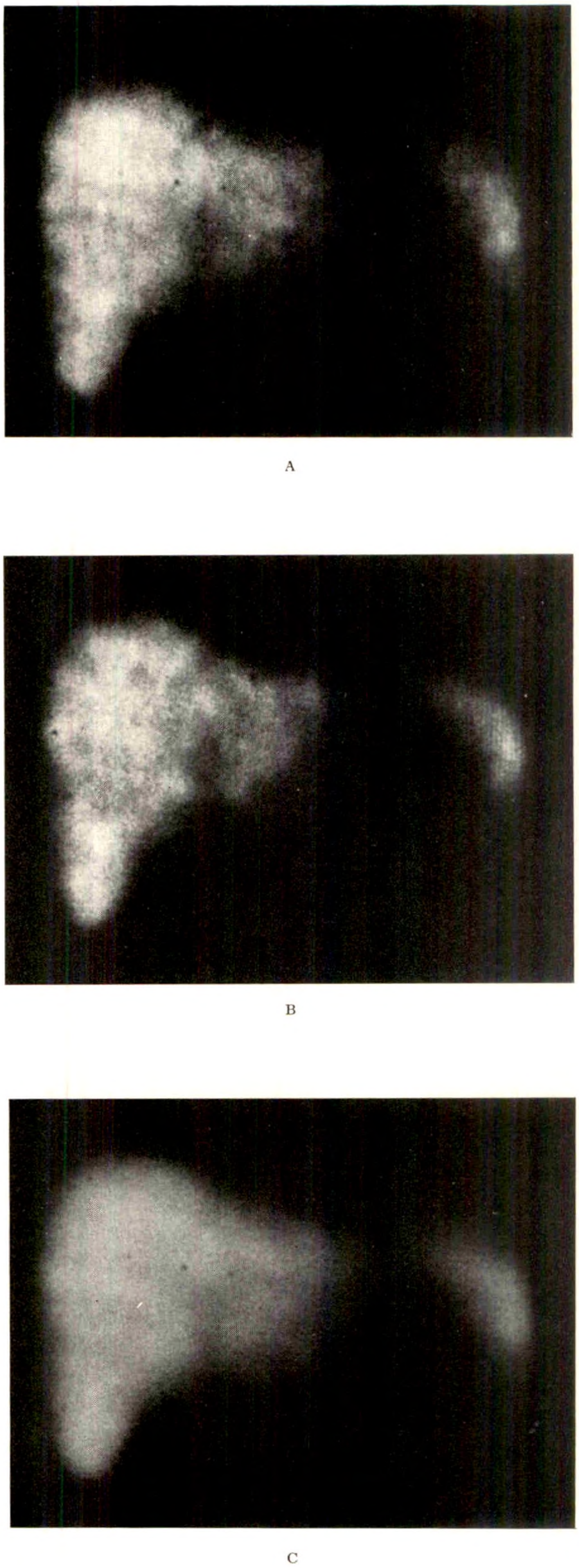


FIG. 5.

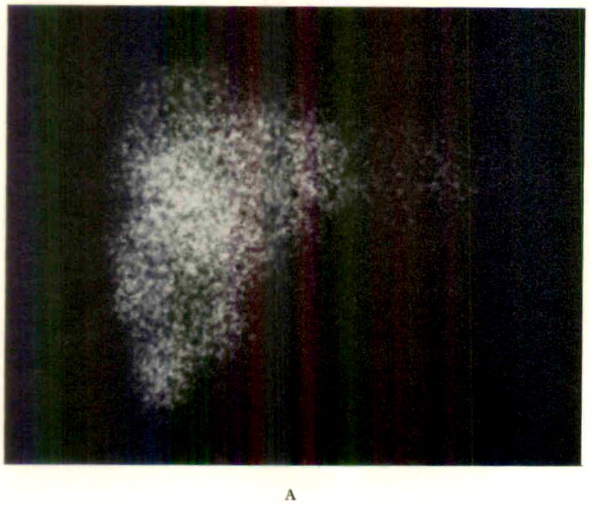
Scan display at 25 isocount levels by linear interpolation (A), processed scan by non-stationary filter (B), and a nine point smoothed scan (C) of a patient with multiple abscesses diagnosed at laparotomy. These are clearly represented by focal defects on the processed scan. The nine point smoothing abolishes the true focal lesions.

assumed on clinical grounds to have secondaries in the liver. Four of these 15 patients died within the six month period and the rest deteriorated with further enlargement of their livers).

The ROC curves drawn for four observers (illustrated here for two, a physician and a physicist, in Figs. 1 and 2) show that processing by a non-stationary filter results in a higher true positive rate than that achieved by the original gamma camera scans, by 25 isocount levels display (produced without smoothing or enhancement) or by displays produced with the use of nine-point smoothing. In fact the nine-point smoothing results in an obvious fall in true positive rate compared to the original gamma camera scan or display of 25 isocount levels (achieved using linear interpolation from $64^2 \rightarrow 128^2$ only). The curves for the gamma camera scans and the 25 isocount levels displays are similar in both Figs. 1 and 2.

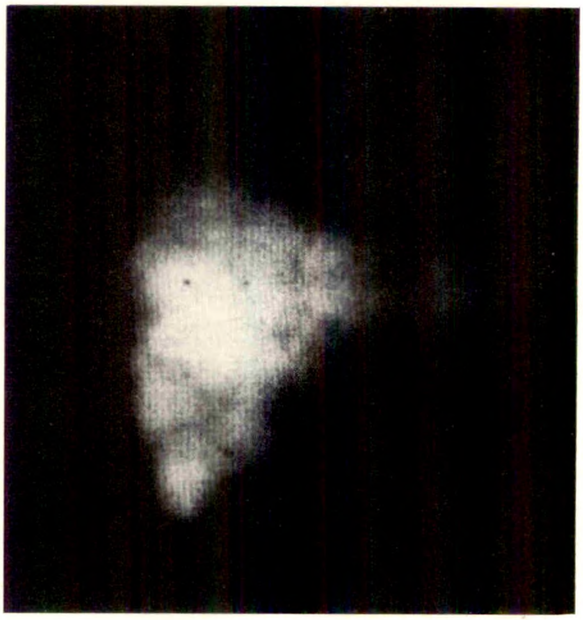
The curves for processed scans are even better when one excludes those of patients who are known to have had chronic liver disease at the time of scanning and those who had clinical signs and symptoms suggestive of chronic liver disease (Figs. 3 and 4). The majority of these patients were known cases of alcoholic cirrhosis, chronic active hepatitis and primary biliary cirrhosis. The curve for processed scans for observer II (physician), for example, reached the ideal position which is a true positive rate of near 100% with a negligible false positive rate (Fig. 4).

The true positive fraction, false positive fraction, true negative fraction and false negative fraction,

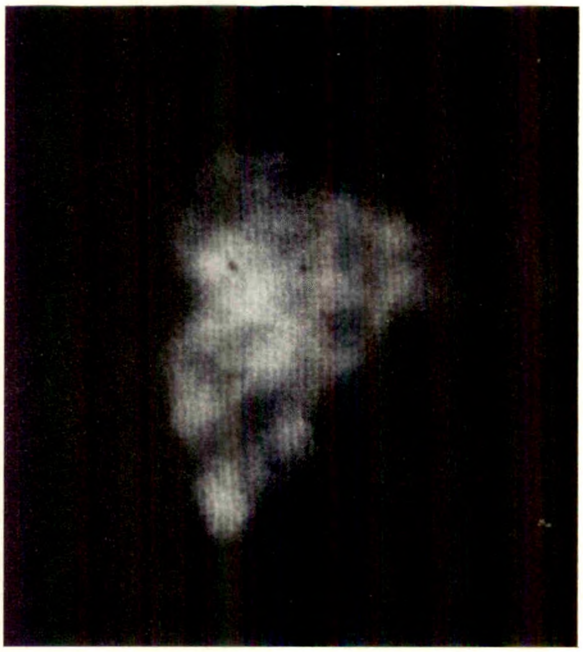


A

FIG. 6.



B



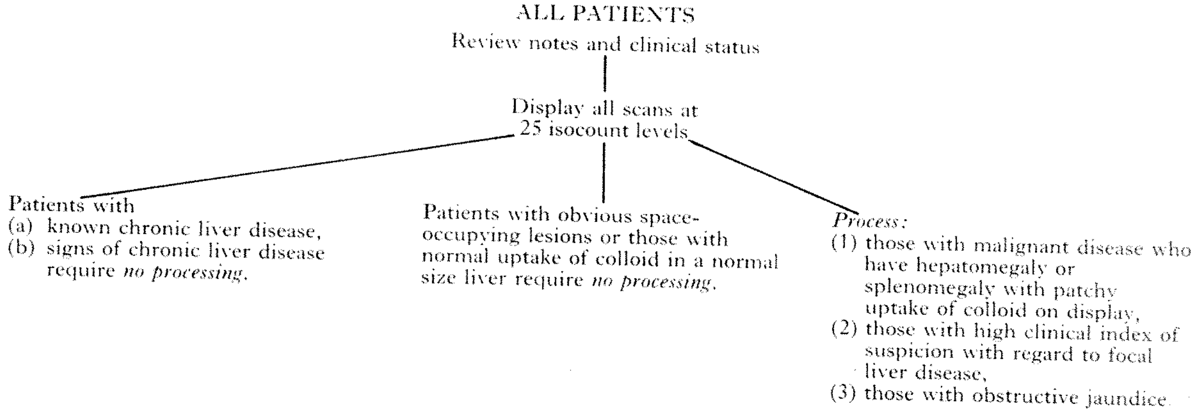
C

FIG. 6.

Gamma-camera scan (A), display by linear interpolation at 25 isocount levels (B), and scan processed by non-stationary filter (C) of a patient with multiple secondaries. Although the focal areas of disease are seen on all three modes of presentation they are most obvious on the processed scan.

TABLE III

CLINICAL STRATEGY FOR THE USE OF COMPUTER PROCESSING OF LIVER SCANS



ALL PATIENTS
Review notes and clinical status

Display all scans at
25 isocount levels

Patients with
(a) known chronic liver disease,
(b) signs of chronic liver disease
require *no processing*.

Patients with obvious space-occupying lesions or those with normal uptake of colloid in a normal size liver require *no processing*.

Process:
(1) those with malignant disease who have hepatomegaly or splenomegaly with patchy uptake of colloid on display,
(2) those with high clinical index of suspicion with regard to focal liver disease,
(3) those with obstructive jaundice.

which were obtained by reporting (by one physician) the scans with "yes" or "no" with regard to a presence of focal liver disease, are represented in Table I. The statistical comparison of true positive values for the various groups is given in Table II.

DISCUSSION

The results of this study analysed using ROC curves show that processing with the use of a non-stationary filter results in scans of greater diagnostic value than ordinary gamma-camera scans or isocount displays obtained without smoothing or enhancement. The scans processed with the filter are even more useful in picking out those cases of multiple focal lesions which produce an appearance of patchy uptake of colloid even on the display of 25 isocount levels (Fig. 5). Lesions which on gamma camera scans or on the display of 25 isocount levels are just about visible are made prominent by the non-stationary filter (Fig. 6). Unfortunately, with processing false focal lesions may be created as suggested by Sebern *et al.* (1976), especially in cases of cirrhosis and liver congestion. As both regenerative nodules producing the appearance of "pseudotumours" in cirrhosis and true space-occupying lesions are focal areas of disease it is not surprising that both are enhanced by the filter. The nine-point smoothing on the other hand not only smooths and gets rid of the "noise" but it also blurs the obvious large lesions and abolishes the small ones (Fig. 5). As a result of this there is a fall in true positive rate.

Our results therefore lead us to suggest that nine-point smoothing is an unsatisfactory method of processing liver scans when the number of counts is 100 k for anterior and posterior views and 80 k for lateral view.

If the computer is to be used efficiently in static imaging a strategy needs to be developed which would increase the accuracy of the liver scanning as well as saving time and money. A recommended plan (Table III) would be to display all scans at 25 isocount levels and process: (i) those who have primary malignancy and have hepatomegaly or splenomegaly with patchy uptake of colloid on gamma camera scans (since in our series hepatomegaly was present in 100% of patients who had secondary malignant involvement of the liver compared to 19% of those who did not ($P<0.001$); and splenomegaly was present in 57% of patients with secondary malignant involvement of liver and in only 13% of those without secondary malignant involvement ($P<0.01$); (ii) those who have a clinical index of suspicion regarding malignant involvement of liver and (iii) cases of obstructive jaundice. In the latter cases, although the most useful investigation might be to carry out dynamic studies with ^{131}I Rose Bengal or ultrasound, if a ^{99}Tc^{m} sulphur colloid scan is performed it should be processed as dilated ducts of extrahepatic obstruction are more obvious on the processed scan than on gamma camera scans (Fig. 7). This strategy would exclude from processing patients with chronic liver disease. If such a strategy obtaining maximum value from processing is to be used, one needs to have available full clinical information from notes as well as from clinical examination at the time of scanning.

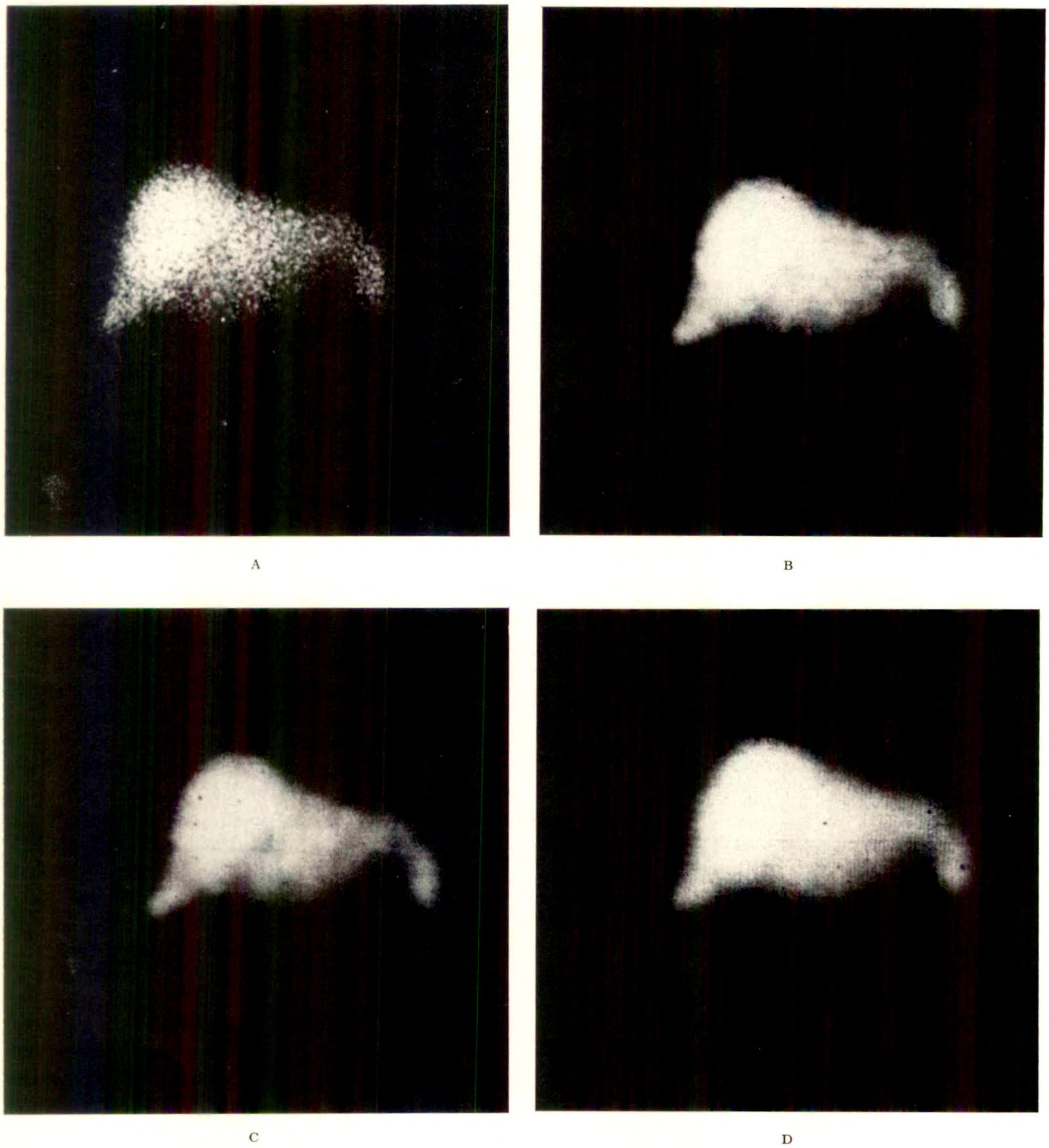


FIG. 7.

Four different presentations of a scan of a patient with extrahepatic obstruction. The central area of reduced uptake is only obvious on the scan processed by the non-stationary filter (C). The gamma camera (A) and 25 isocount levels display by linear interpolation (B) and nine-point smoothed scan (D) do not show this.

ACKNOWLEDGMENTS

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REFERENCES

ALPERT, N. M., CHESLER, D. A., MCKUSICK, K. A., POHOST, G., and BROWNELL, G. L., 1977. *Proceedings of 7th L. H.*

Gray Conference on Medical Images, ed. G. A. Hay, pp. 339–340 (Institute of Physics).

GUSTAFSSON, T. R., and PIZER, S. M., 1976. Non-stationary Metz-filtering. In *Proceedings of IVth International Symposium on Information Processing and Scintigraphy*, eds. C. Raynand and A. Todd-Pokropek, pp. 55–65 (C.E.A., Paris).

KUHL, D. E., SANDERS, T. D., EDWARDS, R. Q., and MALKER, R. J. JR., 1972. Failure to improve observer performance with scan smoothing. *Journal of Nuclear Medicine, 13*, 752–757.

METZ, C. E., STARR, S. J., and LUSTED, L. B., 1977. In *Quantitative evaluation of Medical Images in Medical Radionuclide imaging*, vol. I, pp. 491–499 (I.A.E.A., Vienna).

QUINN, L. J., III, 1972. *Year Book of Nuclear Medicine*, 1972. 8 (Year Book of Medical Publishers Incorporated, Chicago).

RAI, G. S., 1977. M.Sc. thesis, University of London.

RAI, G. S., HAGGITH, J. W., FENWICK, J. D., and JAMES, O., 1977. Computer display and analysis of liver gamma-camera scans. *Gut, 18*, A417.

SEBERN, M. J., HORGAN, J. D., MEADE, R. C., KRONENNETTER, C. M., RUETZ, P. P., and YEH, E.-L., 1976. Minicomputer enhancement of scintillation camera images using fast fourier transform techniques. *Journal of Nuclear Medicine, 17*, 647–652.

TAUXE, W. N., 1968. Digital computer processing of radioisotope scintiscan matrices. *Journal of American Medical Association, 205*, 85–89.

Book review

Technologist Guide to Mammography. Second Edition, By Robert L. Egan, pp. xii+155, 200 illustrations, 1977 (The Williams & Wilkins Company, Baltimore). $18.95.

Over the years Professor Egan has developed and perfected a very personal technique of achieving excellent quality film mammograms. In his view mammography requires no special equipment but demands only meticulous attention to radiographic technique. The most important factors are considered to be "controlled motion, long target-film distance, exquisite collimation and good processing."

The technique recommended is—a kilovoltage range of 20 to 30 KVp; 300mA panel setting; six second exposure time; inherent tube filtration only; A.F.D. of 22 to 40 ins. using an extension type cylinder cone. Industrial type, fine-grain X-ray film should be used and hand processing is advised. A tungsten target tube is considered satisfactory as it is believed that there is no advantage in the use of molybdenum targets in mammography. It is also stated that there is no practical advantage in using beryllium window tubes.

There is no doubt that Professor Egan obtains excellent mammograms and he maintains that the skin dose is of the order of two rads per exposure, a surprisingly low dose in the circumstances. Other mammographic techniques such as film-screen systems, magnification technique and xeroradiography are mentioned briefly but are considered inferior. He believes steadfastly in the superiority of his method.

Radiographic technique is very well described and illustrated in two chapters covering the usual radiographic positions and supplemental views and positions sometimes required. The information in these chapters is extremely useful to all mammographers whether or not the Egan method is employed. The recognition of faulty films is adequately covered and the appearances of normal breasts and the changes found in breast disease are well described. These chapters are unchanged since the first edition.

New material in this second edition includes chapters on breast self-examination and clinical examination of the breast. These are presumably intended for radiographers involved in breast screening programmes. There are new chapters on breast cancer screening and on the benefits versus risks of mammography, in which there is a spirited defence of mammography and scepticism regarding the derivation and calculation of the risk factors.

This book provides interesting reading and great detail regarding the production of conventional film mammograms by strict adherence to a well-tried technique. Much of the material, particularly on radiographic positioning, is useful for other types of mammography also. The reader however is left in no doubt that any deviation from the described technique will only lead to deterioration in the quality of the image produced.

I. H. GRAVELLE

1979, *British Journal of Radiology*, *52*, 124–129

Lymphoscintigraphy: a comparison of ^{99}Tc^{m} antimony sulphide colloid and ^{99}Tc^{m} stannous phytate

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ABSTRACT

In vitro comparison of ^{99}Tc^{m} antimony sulphide colloid and ^{99}Tc^{m} stannous phytate as well as *in vivo* studies in six rabbits and seven patients indicate disparity in the colloidal properties and localization of these two agents. The variability in lymphatic uptake and the relatively poor quality of scintigraphic images following interstitial injection of ^{99}Tc^{m} stannous phytate, when compared with ^{99}Tc^{m} antimony sulphide colloid, provide evidence of the unsuitability of this agent for lymphoscintigraphy. Maintenance of the diagnostic quality of the lymphoscintigraphic image and adherence to interpretive criteria already established therefore preclude the routine use of ^{99}Tc^{m} stannous phytate for interstitial lymphoscintigraphy.

Recent studies (Ege, 1976, 1977) utilizing the subcostal injection of ^{99}Tc^{m} antimony sulphide colloid for visualization of parasternal lymphatics has stimulated an interest in identifying alternative colloids with a small particle size which may be more readily available, more expeditiously prepared, or may improve the quality and specificity of the study.

Similarities in images obtained with colloidal ^{198}Au and ^{99}Tc^{m} Sb sulphide (Ege, 1976) suggest that the common physical property of small, uniform particle size plays a significant part in the effectiveness of the agent. Interstitially injected ^{99}Tc^{m} sulphide colloid presents the drawback of large particles and aggregates, and consequently poor absorption and movement characteristics in the parasternal lymphatics. ^{99}Tc^{m} stannous phytate (^{99}Tc^{m}Sn phytate), developed by Subramanian *et al.* (1973), was described as an *in vivo* formed colloid for imaging the reticuloendothelial system. Localization of the preparation in the bone marrow could be enhanced by increasing the ratio of phytate to tin ion. Assuming that colloids of small particle size localize readily in the bone marrow, it therefore seemed feasible that conditions favouring bone marrow uptake would also provide optimum imaging of the parasternal lymphatics.

The possibility of reducing the particle size of the ^{99}Tc^{m}Sn phytate colloid species formed *in vivo*, by autoclaving the stannous phytate reagent prior to addition of ^{99}Tc^{m} pertechnetate, was investigated by Hamilton *et al.* (1977). They demonstrated that 96% of long-bone deposition was associated with compact bone, and only 4% with bone marrow. This distribution was probably due to heat degradation of the phytate molecule during the autoclaving step, and the subsequent formation of a ^{99}Tc^{m}Sn labelled phosphate moiety with bone-localizing properties.

Clinical comparison of ^{99}Tc^{m}Sn phytate complexed *in vitro* with calcium chloride (Frosst*) and ^{99}Tc^{m} sulphide colloid for liver and spleen imaging was carried out by Arzoumanian *et al.* (1977). They noted a slightly higher background in 33% of the patients studied with the calcium-complexed ^{99}Tc^{m}Sn phytate colloid, and no obvious advantage inherent in this agent other than the short preparative time.

In view of the feasibility of visualizing and assessing lymphatic drainage after the interstitial injection of radiocolloids, the suitability of ^{99}Tc^{m}Sn phytate for lymphoscintigraphy was evaluated and compared with ^{99}Tc^{m}Sb sulphide colloid.

MATERIALS AND METHODS

Preparation of colloids

Stannous phytate kits with a phytate-tin ratio of 20:1 were obtained from New England Nuclear.† In order to standardize the preparation for our studies, all labelled kits were made up to 5 ml.

^{99}Tc^{m}Sb sulphide colloid was prepared by the following modification of the method of Garzon *et al.* (1965). Preformed antimony sulphide reagent was prepared by bubbling hydrogen sulphide gas through 120 ml of boiling sterile distilled water. To this saturated hydrogen sulphide solution, 20 ml of 1% antimony potassium tartrate was added, producing a deep red-orange colour. After adding 10 ml of 3.5% polyvinylpyrrolidone (PVP—mw 40000), nitrogen was bubbled through the solution for

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*Charles E. Frosst & Co., Dorval, Quebec, Canada.

†New England Nuclear Canada Ltd., Montreal, Quebec, Canada.

approximately 30 minutes to remove residual hydrogen sulphide. The solution was tested for the presence of hydrogen sulphide with lead acetate paper, prepared according to the United States Pharmacopoeia method. The preparation was then sterilized by membrane filtration (0.22 μm) into sterile reaction vials for storage. Each reaction vial contained 3 ml antimony sulphide solution, equivalent to 2.35 mg Sb_2S_3.

The preformed colloid was labelled by adding 3 ml sodium pertechnetate ^{99}Tc^{m} to the reaction vial, followed by 0.2 ml 1N HCl. The final pH of the reaction mixture was 1.5. The colloid was then boiled for 30 minutes in a hot water bath. After boiling, the preparation was cooled and 1 ml of a phosphate buffer ($Na_2HPO_4 . 7H_2O$–7.44 g, $NaH_2PO_4 . H_2O$–0.432 g, water to 80 ml) was added to raise the pH to between 6 and 7. The injection volume and activity of both the ^{99}Tc^{m}Sn phytate and ^{99}Tc^{m}Sb sulphide colloid were maintained at 0.1 ml (250 μCi, and less than 0.3 ml (500 μCi) per injection, in animal and patient studies respectively.

Thin-layer chromatography

^{99}Tc^{m}Sn phytate samples were spotted on instant thin-layer chromatography media Type SG and developed in 85% methanol. Samples of ^{99}Tc^{m}Sb sulphide colloid were spotted on Polygram MN

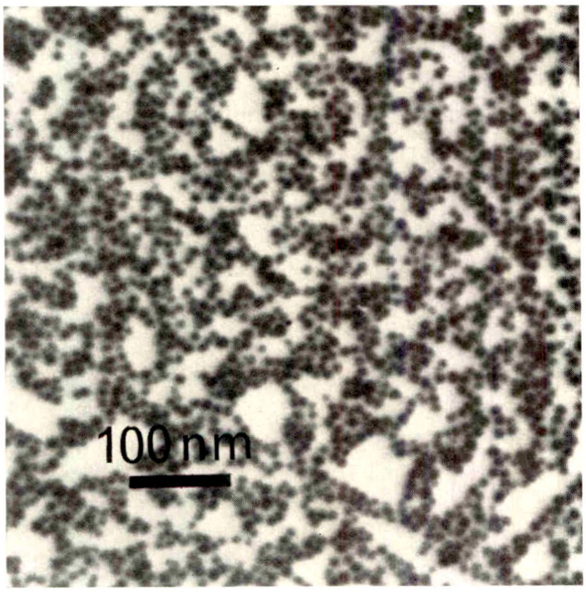

FIG. 1.
Electron micrograph of ^{99}Tc^{m} antimony sulphide colloid.

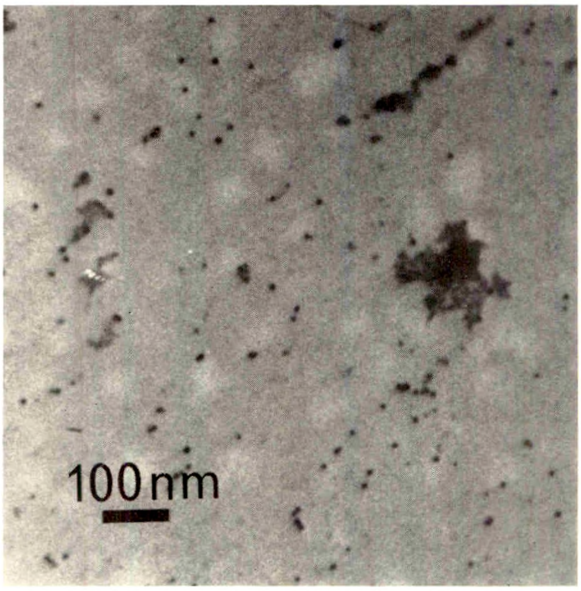

FIG. 2.
Electron micrograph of ^{99}Tc^{m} stannous phytate.

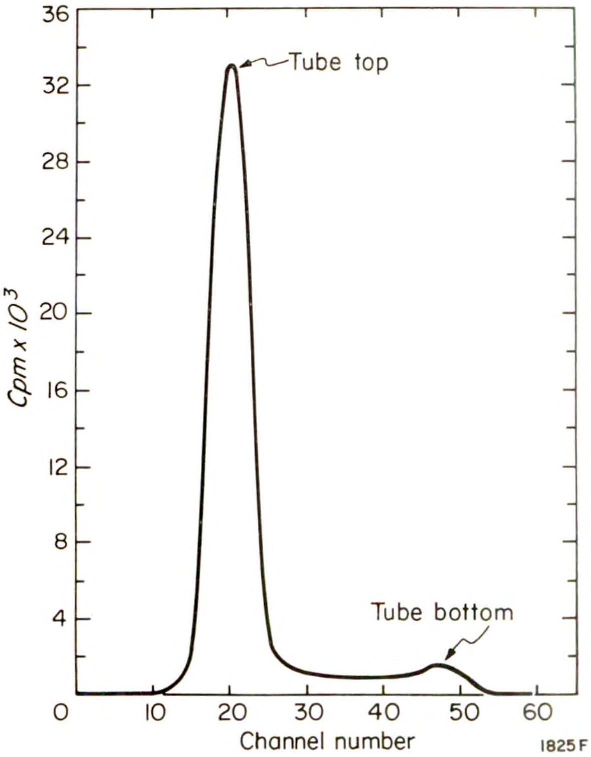

FIG. 3.
Separation of ^{99}Tc^{m} stannous phytate into two components by sedimentation in a 10% sucrose solution.

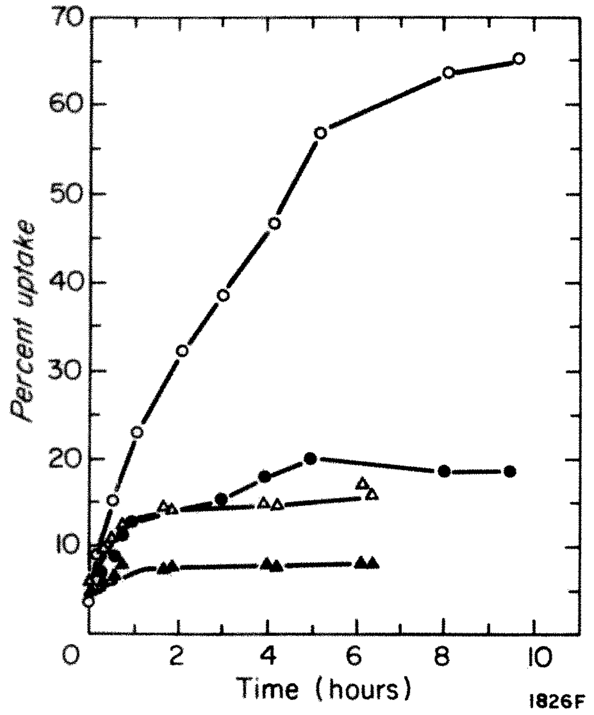

FIG. 4.

Curves comparing *in vivo* distribution in rabbits of ^{99}Tc$^{\mathrm{m}}$ antimony sulphide colloid, indicated by circles, and ^{99}Tc$^{\mathrm{m}}$ stannous phytate, indicated by triangles. ○ △ Total body activity excluding the injection site. ● ▲ Popliteal lymph node activity.

Cellulose 300 media* and developed in 0.9% sodium chloride (Reid, 1976). The chromatographs were run for 10–12 cm, air dried, and cut into strips for counting in an autogamma counter.

Electron microscopy and particle analysis

^{99}Tc$^{\mathrm{m}}$Sn phytate and ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid were spotted on to copper grids (300 mesh) coated with carbon-stabilized plastic (Formvar). The samples were allowed to dry or partially dry and the grid was washed with sterile distilled water to remove any water-soluble salts or contaminants which might interfere with the interpretation of results. The samples were subsequently examined using a transmission electron microscope† (Warbick *et al.*, 1977).

The presence of particles in the samples of ^{99}Tc$^{\mathrm{m}}$Sn phytate were confirmed by centrifugation. The preparation was layered on a 10% sucrose solution and spun at 25000 rpm and 5°C for three hours (SW 41 rotor). ^{99}Tc$^{\mathrm{m}}$ pertechnetate and ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid were run as controls.

APPLICATION

The lymphatic uptake and dynamics of the two preparations were studied in rabbits and patients.

Studies in animals

White New Zealand rabbits weighing 2 kg were injected subcutaneously on the dorsum of the hind foot with 0.1 ml (250 μCi) of ^{99}Tc$^{\mathrm{m}}$Sn phytate or ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid. Three animals were studied with each preparation. The rabbits did not require anaesthesia or restraints during the study. The absorption and movement of colloid into the lymphatics was visualized and measured quantitatively using the Ohio Nuclear 110 Gamma Camera, interfaced to a remote PDP 11/40 computer. Anterior views of the rabbit were taken with the animal resting on the surface of the inverted collimator. Absorption of colloid into the lymphatics was quantitated by measuring the popliteal node uptake in each study. Uptake and counts in the various areas of interest were measured by shielding non-relevant areas. Data obtained by these means were comparable with the information extracted from data stored in a computer.

Studies in patients

In patients with breast carcinoma, we have routinely injected the subcostal site on the side of the primary lesion, documenting any cross drainage pathways with a three hour scintigraphic image. A subsequent contralateral subcostal injection is then performed, and bilateral parasternal lymphatics are visualized six hours after the initiation of the study.

Seven patients were studied with ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid and ^{99}Tc$^{\mathrm{m}}$Sn phytate. The initial injection on the side of the lesion was performed with ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid in order to facilitate investigation of the patients on the basis of criteria developed for interpretation of the parasternal lymphoscintigram utilizing this agent (Ege, 1976). After the three hour scintigram, the contralateral injection was carried out with a similar volume and activity of ^{99}Tc$^{\mathrm{m}}$Sn phytate, and further images obtained three hours later.

RESULTS

The labelling efficiency for both preparations was always greater than 95%. Electron micrographs demonstrate the modal particle size to be 9 nm for ^{99}Tc$^{\mathrm{m}}$Sb sulphide colloid (Fig. 1) and 8 nm for ^{99}Tc$^{\mathrm{m}}$Sn phytate (Fig. 2). Centrifugation of

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*Brinkman Instruments, Inc., Westbury, New York, USA.

†Siemens Elmiskop 102, Iselin, N.J., U.S.A.

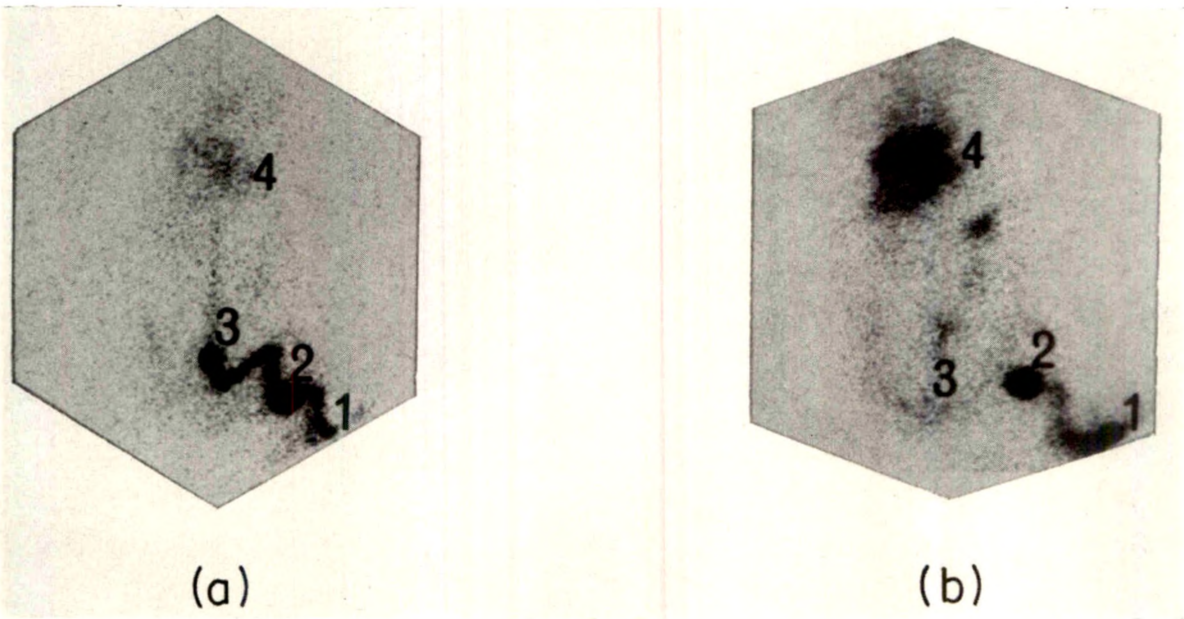

FIG. 5.
A comparison of total body scintigrams obtained 20 minutes after the subcutaneous dorsal hind foot injection of two rabbits with ^{99}Tc^{m} antimony sulphide colloid (a) and ^{99}Tc^{m} stannous phytate (b). 1. Injection site. 2. Popliteal lymph node. 3. Lumbar lymph node. 4. Liver.

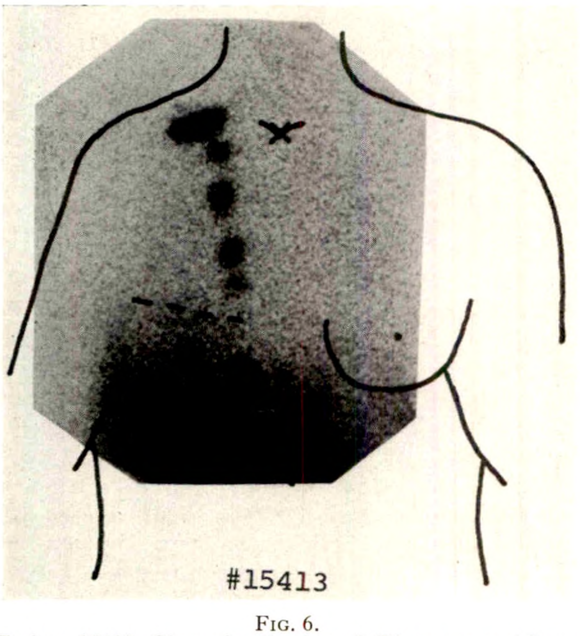

FIG. 6.
Patient 15413. Clear visualization of (R) parasternal lymphatics after (R) subcostal injection of ^{99}Tc^{m} antimony sulphide colloid. There is no comparable visualization of (L) parasternal lymphatics after (L) subcostal injection of ^{99}Tc^{m} stannous phytate.

^{99}Tc^{m}Sn phytate (Fig. 3) showed that 5–10% of the activity in this preparation was associated with these particles. Ionic ^{99}Tc^{m}Sn phytate remained at the top of the sucrose solution while the colloidal component moved down through the sucrose to the base of the tube.

Animal studies showed that the absorption of colloid from the injection site for the two preparations was significantly different. Figure 4 shows the body absorption and popliteal lymph node uptake curves for ^{99}Tc^{m}Sb sulphide colloid and ^{99}Tc^{m}Sn phytate. The curves for ^{99}Tc^{m}Sb sulphide colloid were similar for the three animals studied. The curves for ^{99}Tc^{m}Sn phytate were similar for only two of the rabbits studied. Because of inadequate absorption shown by the third rabbit, the popliteal node could not be visualized for quantitation of radiocolloid uptake. Figure 5 is a comparison of total-body scans taken 20 minutes after injection of the two preparations. Absorption of the phytate preparation from the injection site was less than that observed with ^{99}Tc^{m}Sb sulphide colloid and no uptake was seen in the lumbar node. The higher liver uptake with the phytate preparation was probably due to the rapid movement of ionic ^{99}Tc^{m}Sn phytate through the

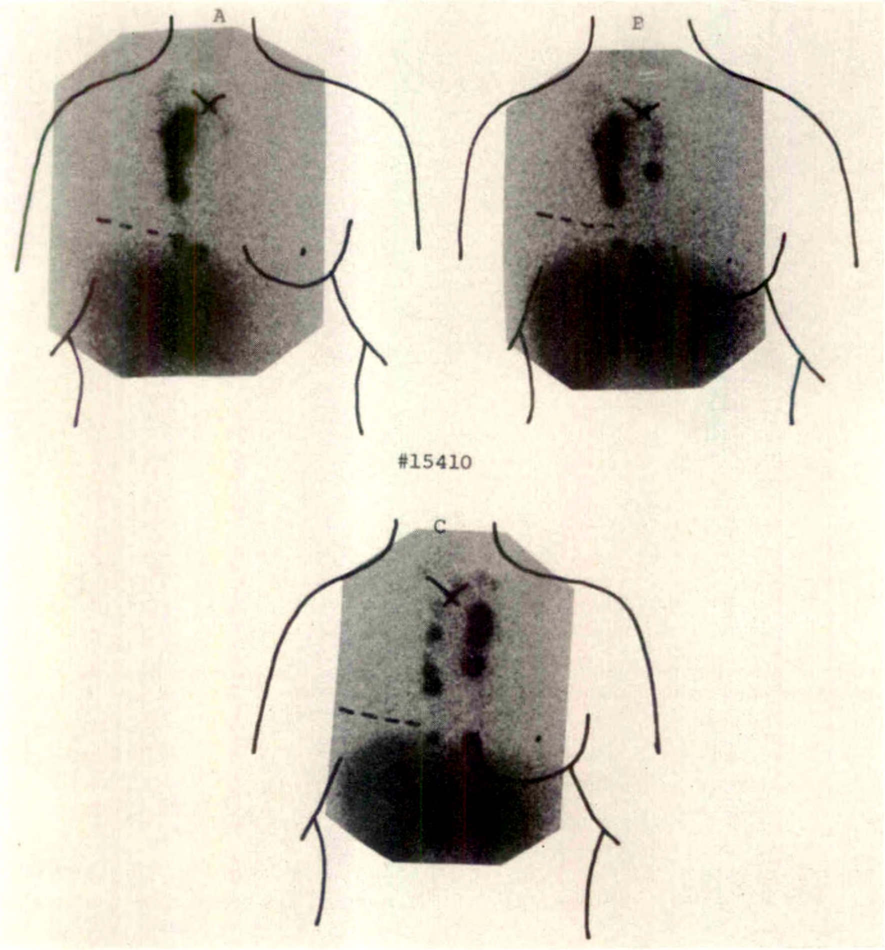

Fig. 7.

Patient 15410. (A) Lymphoscintigram three hours after (R) subcostal injection of ^{99}Tc^{m} antimony sulphide colloid. (B) Image obtained three hours after subsequent (L) subcostal injection of ^{99}Tc^{m} stannous phytate. (C) Study six weeks later after (R) subcostal injection of ^{99}Tc^{m} stannous phytate and (L) subcostal injection of ^{99}Tc^{m} antimony sulphide colloid. Note consistent difference in quality of lymphatics demonstrated by both agents.

lymphatic pathway and the consequent formation of calcium complexed ^{99}Tc^{m}Sn phytate as the preparation emptied into the vascular system at the jugulo-subclavian junction.

In patients, the majority of the images showed very poor delineation of the lymphatics draining the ^{99}Tc^{m}Sn phytate injection site. The diaphragmatic node closest to the site of injection, invariably appearing very prominent following the ^{99}Tc^{m}Sb sulphide colloid injection, demonstrated poor uptake of activity with phytate and in most patients was barely visible (Fig. 6). In only one patient was there satisfactory radiocolloid uptake in the lymphatics draining the site of ^{99}Tc^{m}Sn phytate injection (Fig. 7), but the contrast between this chain and the contralateral ^{99}Tc^{m}Sb sulphide colloid chain is very apparent. This study was repeated six weeks later, the injection media alternated, and again the contrast between ^{99}Tc^{m}Sn phytate and ^{99}Tc^{m}Sb sulphide colloid was readily recognized.

Discussion

Animal studies with the two colloids showed decreased uptake of ^{99}Tc^{m}Sn phytate as compared with the rapid and reproducible uptake of ^{99}Tc^{m}Sb sulphide colloid. Although ^{99}Tc^{m}Sn phytate has been reported to yield satisfactory parasternal lymphoscintigrams (Kaplan *et al.*, 1977, unpublished), in our experience lymph node visualization has been inconsistent and inferior to studies carried out with $^{99}\mathrm{Tc^{m}}$Sb sulphide colloid. Radiocolloid uptake when seen in nodes was not as intense, providing less information regarding lymphatic integrity. This may be due to the absorption of a smaller number of particles from the injection site. The possibility of formation of a calcium-complexed phytate colloid at the injection site should be considered.

Alavi *et al.* (1978), using $^{99}\mathrm{Tc^{m}}$Sn phytate in animal models, indicate high extranodal concentration in liver, spleen, kidney and bladder, as well as increased body background. The poor target-to-background ratio inherent in $^{99}\mathrm{Tc^{m}}$Sn phytate suggests that interstitially injected $^{99}\mathrm{Tc^{m}}$Sb sulphide colloid is superior to $^{99}\mathrm{Tc^{m}}$Sn phytate and is at present the colloid of choice for interstitial lymphoscintigraphy.

CONCLUSION

The feasibility of labelling different compounds and complexes with $^{99}\mathrm{Tc^{m}}$ has provided great versatility in clinically utilizable agents. It must be appreciated, however, that each agent has unique features which may not be duplicated by any other agent, despite apparent similarities, and unless such limitations are recognized the substitution of another agent may jeopardize the quality and accuracy of the study. In view of their diverse properties, the substitution of $^{99}\mathrm{Tc^{m}}$Sn phytate for $^{99}\mathrm{Tc^{m}}$Sb sulphide colloid in interstitial lymphoscintigraphy is not recommended.

ACKNOWLEDGMENTS

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REFERENCES

EGE, G. N., 1976. Internal mammary lymphoscintigraphy—the rationale, technique, interpretation and clinical application: a review based on 848 cases. *Radiology, 118*, 101–107.

1977. Internal mammary lymphoscintigraphy in breast carcinoma: a study of 1072 patients. *International Journal of Radiation Oncology Biology Physics, 2*, 755–761.

SUBRAMANIAN, G., MCAFEE, J. G., MEHTA, A., BLAIR, R. J., and THOMAS, E. D., 1973. Tc-99m stannous phytate: a new *in-vivo* colloid for imaging the reticuloendothelial system. *Journal of Nuclear Medicine, 14*, 459.

HAMILTON, R. G., ALDERSON, T. L., and MCINTYRE, P. A., 1977. Tc-99m phytate as a bone-marrow imaging agent: biodistribution studies in animals. Concise communication. *Journal of Nuclear Medicine, 18*, 563–565.

ARZOUMANIAN, A., ROSENTHALL, L., and SETO, H., 1977. Clinical comparison of Tc-99m labelled preformed phytate colloid and sulphur colloid. Concise communication. *Journal of Nuclear Medicine, 18*, 118–120.

GARZON, O. L., PALCOS, M. C., and RADICELLA, R., 1965. A technetium-99m labelled colloid. *International Journal of Applied Radiation and Isotopes, 16*, 613.

REID, B. D., 1976. Personal communication.

WARBICK A., EGE, G. N., HENKELMAN, R. M., MAIER, G., and LYSTER, D. M., 1977. An evaluation of radiocolloid sizing techniques. *Journal of Nuclear Medicine, 18*, 827–834.

KAPLAN, W. D., DAVIS, M. A., and ROSE, C. R., 1977. Internal mammary lymphoscintigraphy with 99m-Tc labelled stannous phytate and antimony sulfide: a clinical evaluation (unpublished).

ALAVI, A., STAUM M. M., SHESOL, B. F., and BLOCH, P. H., 1978. Technetium-99m stannous phytate as an imaging agent for lymph nodes. *Journal of Nuclear Medicine, 19*, 422–426.

Book review

A Guide to Medical Ultrasonics and Acoustics. Hospital Physicists Association Scientific Report Series, No. 10, pp. 44, 1977. (Hospital Physicists Association, London), £2·00.

Acoustics is still a subject in which many medical physicists feel ill at ease and this little booklet is designed to introduce them to some of the basic ideas and to provide them with the beginnings of a bibliography. It necessarily spans a wide range of material in a limited space—two or three pages each to cover such topics as audiology, Doppler measurement of blood velocity, imaging, ultrasonic surgery and the "biological safety" of ultrasound—but, within this limitation, it should prove very useful. In any subsequent edition it would be helpful to include reference to some of the more detailed general books and articles on the subject which are now starting to proliferate.

C. R. HILL.

1979, *British Journal of Radiology*, 52, 130–133

High thyroid radiation dose associated with ^{131}I-19-iodocholesterol adrenal scanning

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ABSTRACT

We have examined two patients undergoing ^{131}I-19-iodocholesterol adrenal scans in order to assess thyroidal radiation dose. Thyroid uptakes of 3–5% of the administered 2 mCi dose were found despite prior administration of Lugol's iodine. Analysis of serum samples over a ten day period after iodocholesterol injection indicated that less than 10% of the radioactivity was free iodide. Kinetic results showed a high value for the thyroid/plasma ^{131}I ratio indicating thyroid retention of ^{131}I. This was substantiated by thyroid scintigrams. The thyroid radiation dose was estimated to be 200–250 rad for the two patients. The associated carcinogenic risk is of sufficient magnitude, in our opinion, to warrant regular follow-up of all patients who have undergone ^{131}I-19-iodocholesterol adrenal scanning.

Radionuclide imaging of the adrenal gland using ^{131}I-19-iodocholesterol has been successfully used in the localization of adrenal lesions (Lieberman *et al.*, 1971; Conn *et al.*, 1972; Sturman, *et al.*, 1974). The use of this radiopharmaceutical has been regarded as a safe diagnostic procedure with an acceptable radiation dose when balanced against the hazards of adrenal venography (Kirschner *et al.*, 1973; Charbonnel *et al.*, 1976). However, in studies on two patients we have found that this radiopharmaceutical delivered a radiation dose to the thyroid which greatly exceeded that expected; on the basis of these findings we believe that this warrants a reappraisal of the merits of this scanning agent.

ADRENAL SCAN PROCEDURE

Patients were scanned using ^{131}I-iodocholesterol (19-iodocholest-5 en-3-ol) obtained through Sorin§ and with a stated purity of 94.6%. A dose of 2 mCi of ^{131}I-iodocholesterol was administered intravenously and the patient scanned at regular intervals during a ten day period. Thyroidal uptake of free iodide was blocked by administration of Lugol's iodine (five drops twice daily) two days prior to and for the duration of the scanning procedure. Thyroid scans were carried out in the two patients using ^{99}Tc^{m} pertechnetate.

CASE REPORTS

Case 1

Prior to surgery an adrenal ^{131}I-iodocholesterol scan was performed on a 23-year-old woman with Cushing's syndrome. During the scanning period the level of ^{131}I in the thyroid was monitored and quantitated (Table I). Measurements were carried out using a standard uptake probe and methodology as recommended by the IAEA (1962), corrections being made for extrathyroidal neck activity using the method of Goolden and Mallard (1958). Sufficient ^{131}I was found in the thyroid to permit scanning of the gland and a scan performed eight days post-injection (Fig. 1C) was similar to that obtained with ^{99}Tc^{m} (Fig. 1D) and demonstrated that the ^{131}I was concentrated within the gland with little extrathyroidal neck activity.

TABLE I

KINETIC AND DOSIMETRIC DATA FOR ^{131}I-19-IODOCHOLESTEROL IN THE TWO CASES STUDIED. BIOLOGICAL HALF LIFE ($T_{1/2}$ BIOL) IS SHOWN FOR THYROID, PLASMA AND URINE

	$T_{1/2}$ biol (days)			Maximum thyroid uptake		Estimated gland mass (g)
	1st component	2nd component	Average			
				μCi	%	
Case 1						
Thyroid	2.6 (55.5%)	16 (44.5%)	6.2	78	3.9	20
Case 2						
Thyroid	1.5 (68.6%)	7.3 (31.4%)	3.3	93	4.9	15
Plasma	1.5 (70.7%)	2.8 (29.3%)	1.9	—	—	—
Urine*	1.0 (78.3%)	2.1 (21.7%)	1.2	—	—	—

*Note: Urinary $T_{1/2}$ biol calculated from % administered dose per day.

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§Sorin Biomedica, 13040 Saluggia, Italy.

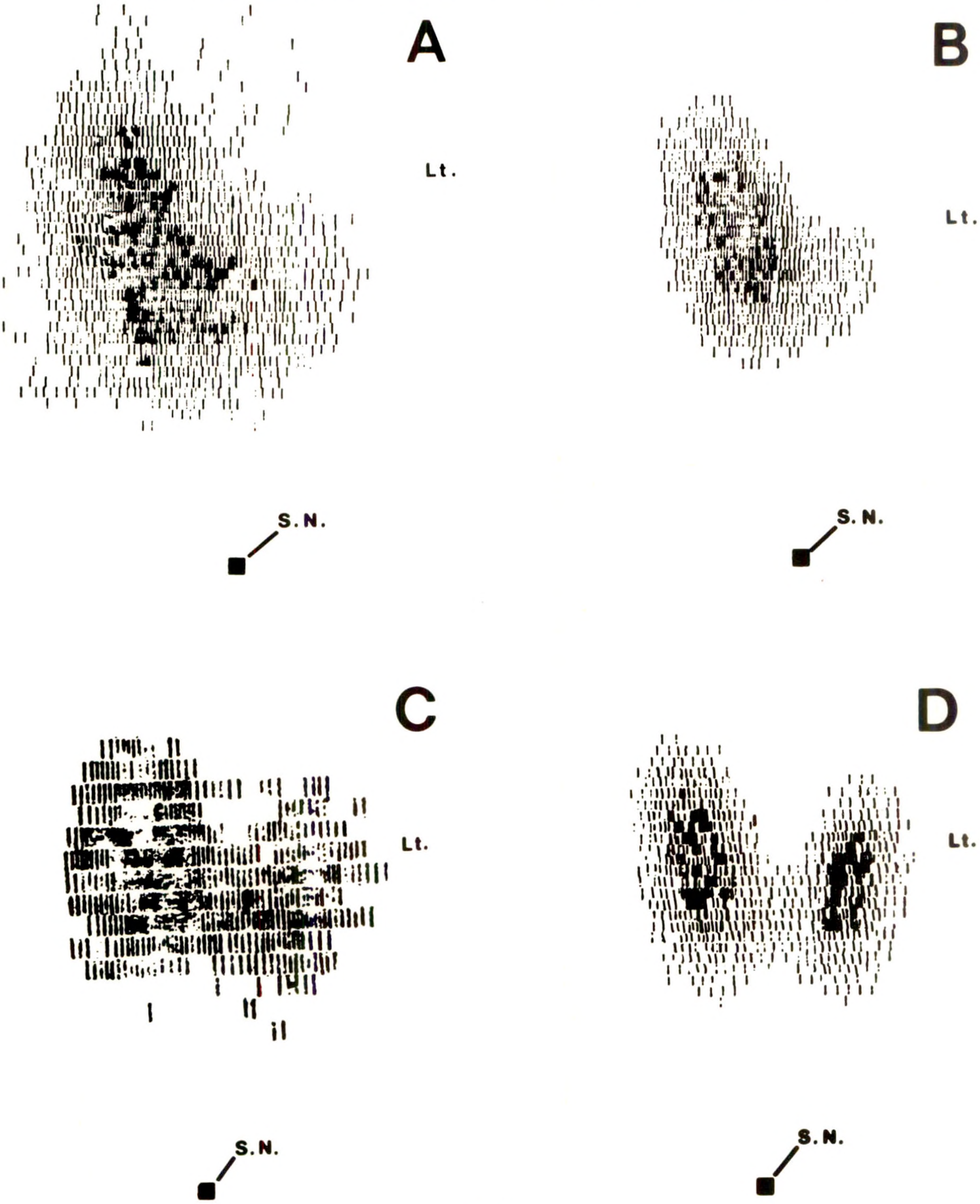

FIG. 1.

(A) Case 2, 2 mCi ^{131}I-iodocholesterol scan of the thyroid two days post-injection.
(B) Case 2, 2 mCi ^{99}Tc^{m} pertechnetate scan 30 min post-injection.
(C) Case 1, 2 mCi ^{131}I-iodocholesterol scan of the thyroid eight days post-injection.
(D) Case 1, 2 mCi ^{99}Tc^{m} pertechnetate scan of the same gland 30 min post-injection.

TABLE II

Behaviour of serum samples (Case 2) applied to QAE anion-exchange column

Sample applied to column	% activity in column	No. of samples
Pre-injection serum + ^{131}I	< 1.0%	2
Pre-injection serum + ^{131}I-iodocholesterol	70.5 ± 13.4%	2
Pre-injection serum + ^{125}I-T_4	3.7 ± 0.4%	2
Post injection serum	76.7 ± 4.2%	10

Case 2

Scanning of the adrenals and testes were requested for a 22 year old man with elevated estradiol levels. In the light of the previous case the patient's thyroid status was evaluated prior to commencement of the adrenal scan. He was found to have a normal 24 hour radioactive iodine uptake of 33%, after which the gland was blocked with Lugol's as in the previous case. A repeat measurement of iodine uptake at 24 hours was 2–3%. Although the ^{99}Tc^{m} pertechnetate scan demonstrated an asymetrical gland (Fig. 1B), the patient was clinically and biochemically euthyroid with no palpable thyroid and it was concluded that this was not a warm nodule.

After injection of ^{131}I-iodocholesterol high thyroidal levels of ^{131}I were again found (Table I) and a ^{131}I scan obtained two days post-injection (Fig. 1A) was in agreement with that obtained with ^{99}Tc^{m} pertechnetate (Fig. 1B).

Quantitative measurement of the ^{131}I activity in the serum and urine was carried out daily for ten days post injection (Table I). Analysis of serum samples using an iodide extraction resin (Iobeads-Technicon Ltd.,) showed that free iodide accounted for 13% of the total radioactivity over the first 48 hours and approximately 4% thereafter. Further analysis of the serum radioactivity was performed on a QAE anion-exchange resin column modified slightly from the method of Burger (1974). The behaviour of the serum samples applied to the column are shown in Table II. These results indicate that for the most part serum radioactivity behaved like iodocholesterol or a metabolite thereof.

Absolute measurements of serum and urine activity showed that the serum ^{131}I activity on day one was 3.82% dose/litre and the cumulative urine activity was 32.4% dose after one day rising to 76.6% after ten days.

Discussion

Despite its widespread use, the paucity of data on human metabolism of ^{131}I-19-iodocholesterol is emphasized by the existence of only one report to date by Kirschner *et al.* (1973) on its turnover in humans. We have compared our results (Table I) with those calculated from Kirschner's data over the ten-day period following injection. From their data on six patients we have calculated the serum $T_{1/2}$ biol (first component) to be 1.3±0.3 day compared to our value of 1.5 days. In only one patient were data obtained for nine days and this shows a second component $T_{1/2}$ biol of 2.5 days compared to our 2.8 days. Thus we have found identical serum decay curves and comparable whole-body retention estimates based on urine data (no data obtained on faeces). Furthermore an examination of thyroidal retention and serum figures shows that after five days there is a clear increment in thyroid/serum ratios indicating thyroidal retention of ^{131}I. Recently Seabold *et al.* (1977) have shown considerable quantities of ^{131}I in the thyroids of patients undergoing ^{131}I-iodocholesterol (^{131}I-6-β-iodomethyl-19-norcholesterol) whole-body scanning for metastatic adrenal carcinoma.

In the two patients studied here the thyroidal uptake of ^{131}I was approximately 3–5% with little extrathyroidal neck activity (Fig. 1A and 1C). To explain this degree of uptake on the basis of free iodide alone and with the thyroid under effective Lugol's block, the serum radioactivity would need to be 100% free iodide. Barbarino *et al.*, (1975) have examined the effect of various blocking agents on thyroidal uptake of ^{131}I following adrenal scanning with ^{131}I-iodocholesterol. They found uptakes of 8% in a patient blocked with Lugol's and uptakes of between 5.8% and 10.8% in four patients blocked with Lugol's+triiodothyronine. However, in eight patients whose thyroids were blocked with potassium perchlorate ($KClO_4$) the uptakes were between 0.5% and 1.8%.

A possible explanation for these findings is that iodocholesterol is taken up and de-iodinated in the thyroid to release I^- available for organification. After de-iodination $KClO_4$ may be more effective in discharging the free iodide than Lugol's. Nonetheless uptake of iodocholesterol initially seems likely.

As a result of this uptake the radiation dose to the thyroid was 200 rad (Case 1) and 230 rad (Case 2) calculated by the method of Quimby *et al.* (1970). For thyroidal doses in this range, estimates of the magnitude of the carcinogenic risk involved vary, but lie between two and ten cases per million man-years follow-up per rad (Conard, 1973; BEIR Report, 1974; Modan *et al.*, 1977), based on data obtained from groups irradiated during childhood. Excess thyroid cancers have also been associated with irradiation in adults, and are thought to be quite likely in those whose thyroids come under humoral stimulation (Berson and Yalow, 1952; Doniach *et al.*, 1966), although reliable risk estimates are not available. The population subjected to adrenal scans are unlikely to be endocrinologically normal and may be unusual with regard to the likelihood of their thyroid being subject to stimulation over a long follow-up period. While it is likely to be an overestimate it is nevertheless of interest to calculate the worst possible risk based on the childhood irradiation data, assuming a value of 5×10^{-6} per man-year per rad. In the above cases this would give rise to risks of carcinogenesis over a

50 year follow-up period of 5.1% and 5.7% respectively. Since radiation-induced benign nodules occur at about ten times the rate of carcinomas (Conard, 1973), the corresponding risk estimates in the above two cases are 51% and 57% respectively. The magnitude of these risks, admittedly worst possible estimates, is such that they warrant thyroid follow up in these patients. From the work of Barbarino *et al.* (1975) it appears that satisfactory reduction of the thyroidal radiation dose can be achieved by the prior administration of $KClO_4$. Furthermore, in patients who cannot be given $KClO_4$ due to side effects from this drug the above arguments based on radiation dose will probably be less serious with the availability of alternative adrenal scanning radiopharmaceuticals (Sarkar *et al.*, 1976).

In conclusion, because of the importance of complete kinetic data on any radiopharmaceutical in humans we believe that further work is necessary on any proposed cholesterol labelled scanning agents.

REFERENCES

BARBARINO, A., TRONCONE, L., SALVO, D., and PASARGIKLIAN, E., 1975. Thyroidal accumulation of ^{131}I during adrenal gland scintigraphy with ^{131}I-iodocholesterol: effects of thyroid blocking agents. *Journal of Clinical Endocrinology and Metabolism, 41*, 405–407.

BEIR Report, 1974. The effect on populations of exposure to low levels of ionizing radiation. *National Academy of Sciences, 45*, 582–612: (US Government Printing Office, Washington, DC).

BURGER, A., 1974. *Thyroxine Radioimmunoassay, Clinical Biochemistry-Principles and Methods*, eds. H. Curtis and M. Roth, pp. 881–883 (Berlin, Walter de Gruyter).

CHARBONNEL, B., CHATAL, J., CHUPIN, M., and GUILLON, J., 1976. Interet de la scintigraphic surrenalienne au ^{131}I-19-iodocholesterol dans l'exploration des syndromes de Cushing, *Annales d'Endocrinologie, 37*, 315–316.

CONARD, B. A., 1973. A twenty year review of medical findings in a Marshallese population accidentally exposed to radioactive fallout (BNL 50424 Brookhaven National Laboratory, New York).

CONN, J., MORITA, R., COHEN, E., BEIERWALTES, W. H., McDONALD, W. J., and HERWIZ, K. R., 1972. Primary aldosteronism: photoscanning after administration of ^{131}I-19-iodocholesterol. *Archives of Internal Medicine, 129*, 417–425.

DONIACH, I., EADIE, D. G. A., and HOPE-STONE, H. F., 1966. The development of multiple thyroid adenomata in primary hyperthyroidism in previously irradiated thyroid glands. *British Journal of Surgery, 53*, 681–685.

GOOLDEN, A. W. G., and MALLARD, J. R., 1958. A method of correction for extrathyroidal activity. *British Journal of Radiology, 31*, 41–44.

International Atomic Energy Agency, 1962. Consultants meeting on the calibration and standardisation of thyroid radioiodine uptake measurements, 1960. *British Journal of Radiology, 35*, 205–210.

KIRSCHNER, A. S., ICE, R. D., and BEIERWALTES, W. H., 1973. Radiation dosimetry of ^{131}I-19-iodocholesterol. *Journal of Nuclear Medicine, 14*, 713–717.

LIEBERMAN, L. M., BEIERWALTES, W. H., CONN, J. W., and NISHIYAMA, H., 1971. Diagnosis of adrenal disease by visualization of human adrenal glands with ^{131}I-19-iodocholesterol. *New England Journal of Medicine, 285*, 1387–1393.

MODAN, B., RON, E., and WERNER, A., 1977. Head and neck tumours and impaired mental function following scalp irradiation. *Proceedings I.R.P.A.*, 723–725.

QUIMBY, E. H., FEITELBERG, S., and GROOS, W., 1970. Dosage calculations for radioactive nuclides. *Radioactive Nuclides in Medicine and Biology*, pp. 102–139. (Lea and Febiger, Philadelphia).

SARKAR, S. D., ICE, R. D., BEIERWALTES, W. H., GILL, S. P., BALACHANDRAN, S., and BARMADJIAN, G. P., 1976. Selenium-75-19-Selenocholesterol- a new adrenal scanning agent with high concentration in the adrenal medulla. *Journal of Nuclear Medicine, 17*, 212–217.

SEABOLD, J. E., HAGNIE, T. P., DE ASIS, D. N., SAMAAN, N. A., GLENN, H. J., and JAHNS, M. F., 1977. Detection of metastatic adrenal carcinoma using ^{131}I-6-β-iodomethyl-19-Norcholesterol total body scans. *Journal of Clinical Endocrinology and Metabolism, 45*, 788–797.

STURMAN, M. F., MOSES, D. C., BEIERWALTES, W. H., HARRISON, T. S., ICE, R. D., and DORR, R. P., 1974. Radiocholesterol in adrenal images for the localization of pheochromocytoma. *Surgery, Gynecology and Obstetrics, 138*, 177–180.

Book review

Directory of Cancer Research Information Resources. US Department of Health Education & Welfare, National Technical Inorfmation Service, Virginia, USA, pp. x+226, Domestic orders $8.00 (paper back), $3.00 (microfiche). Non-domestic orders $16.00 (paper back), $4.50 (microfiche).

This is an international list of sources of information on cancer which includes the journals with a main interest in cancer topics, cancer registries, libraries and information retrieval services. Very clearly indexed, and with sufficient detail to provide postal access, this is of particular value to research workers in medical education or epidemiology. The journal section lists the editor, publisher, annual subscription and presentation. There are inevitable omissions of some of the inter-disciplinary journals. The registry list is similarly not exhaustive but does name at least a central contact for each country with such a registry.

A very valuable "not to be removed" addition to any medical library.

A. W. PREECE.

1979, *British Journal of Radiology*, 52, 134–137

A single injection technique for subtraction of blood background in ^{131}I-hippuran renograms

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ABSTRACT

A method of subtracting blood background during probe-renography is presented which does not require a prior injection of RIHSA and which produces results approximately 11% higher than the RIHSA method. The new method treats the renogram up to two-and-a-half minutes as a combination of a fraction of the blood curve and a fraction of the integral of the blood curve. Analysis of the data, using either a computer or a programmed calculator, enables these two fractions to be calculated, hence producing the "background subtraction factor" and the "uptake constant".

One problem in the interpretation of probe-renography arises from the contribution of radioactivity from the blood and tissues surrounding the kidney, the "blood background". In order to compensate for this, a fraction of the blood curve is subtracted from the observed renogram, and there are several methods available for determining this fraction. Possibly the most widely accepted and theoretically the most valid method is the use of an initial injection of ^{131}I human serum albumen (RIHSA), as outlined by Britton and Brown (1971).

Other approaches to the problem of blood-background subtraction involve the use of a γ-camera computer system with "region of interest" background subtraction (Diffey *et al.*, 1976); or subtracting the "vascular spike" of the renal retention function (Kenny *et al.*, 1975; Reeve *et al.*, 1975). Although both the methods involve only a single injection the former is not applicable to probe studies, and both require a computer.

A method has been devised, called the single injection technique (SIT), which obtains the "blood-background subtraction factor", thus saving the patient a second injection, reducing radiation dosage to the patient, and facilitating repeat studies. The single injection technique can be used with either a computer or a programmable desk calculator, and also gives an index of relative renal function.

THEORY

Up to 150 seconds after the injection of ^{131}I hippuran there is no significant excretion from the kidney, so that radioactivity in the kidney is proportional to the integral of the blood curve. In addition to this, the renal detector will also detect activity from tissues surrounding the kidney, and this activity may be represented as a fraction of the blood curve:

$$R(\mathrm{t})=F.B(\mathrm{t})+K\textstyle\int_0^{\mathrm{t}} B(\mathrm{t})\mathrm{dt} \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where $R(\mathrm{t})$ is the activity measured by the renal detector, $B(\mathrm{t})$ is the activity in blood, F is the blood-background subtraction factor relating to the activity in tissue surrounding the kidney, and K is the uptake constant; the factor of activity taken up by the kidney from the blood per unit time. This is easily converted to

$$\frac{R(\mathrm{t})}{B(\mathrm{t})}=F+\frac{K}{B(\mathrm{t})}\int_0^{\mathrm{t}} B(\mathrm{t})\,\mathrm{dt} \quad \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

As this is the equation of a straight line, when $\frac{R(\mathrm{t})}{B(\mathrm{t})}$ is plotted against $\int_0^{\mathrm{t}}B(\mathrm{t})\mathrm{dt}/B(\mathrm{t})$ the intercept will be F, the blood-background subtraction factor. The slope will be K, the uptake constant to the kidney.

The renogram corrected for background is obtained by subtracting F times the blood curve from the renal detector curve. Up to 150 seconds, this corrected renogram will be proportional to the integral of the blood curve.

$$CR(\mathrm{t})=R(\mathrm{t})-F.B(\mathrm{t})=K\textstyle\int_0^{\mathrm{t}}B(\mathrm{t})\mathrm{dt} \quad \ldots\ldots\ldots (3)$$

where $CR(\mathrm{t})$ represents the renogram corrected for blood-background.

The background-corrected renogram may also be considered as a convolution of the blood curve and the impulse function:

$$CR(\mathrm{t})=\textstyle\int_0^{\mathrm{t}}B(\mathrm{t}-T)H(T)dT \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

where $H(\mathrm{t})$ is the impulse function.

Equations 3 and 4 may be combined:

$$K\textstyle\int_0^{\mathrm{t}}B(\mathrm{t})\mathrm{dt}=\int_0^{\mathrm{t}}B(\mathrm{t}-T)H(T)dT \quad \ldots\ldots\ldots\ldots\ldots (5)$$

An analytical solution to equation 5 may be obtained by taking Laplace transforms:

$$K.IB(\mathrm{s})=B(\mathrm{s}).H(\mathrm{s}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

where $B(\mathrm{s})$, $H(\mathrm{s})$ and $IB(\mathrm{s})$ are the Laplace transforms of $B(\mathrm{t})$, $H(\mathrm{t})$ and $\int_0^{\mathrm{t}}B(\mathrm{t})\mathrm{dt}$ respectively. Equation 6 may be converted to:

$$H(\mathrm{s})=K\frac{IB(\mathrm{s})}{B(\mathrm{s})} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

which on taking inverse Laplace transforms gives the solution

$$H(\mathrm{t})=K.T \quad \ldots\ldots(8)$$

where T is the time interval between individual points on the curves. This indicates that the uptake constant K, obtained by applying equation 2, may be compared with its theoretical value which may be obtained by deconvolution analysis up to 150 seconds.

As this single injection technique relies on straight line fitting, it is now possible to compare the intercept (with the RIHSA derived background subtraction factor), and the slope (with deconvolution analysis), and thus test the validity of the method.

METHOD

Renogram data were obtained from the Middlesex Hospital (punch tape data from 20 patients) and the Manchester Royal Infirmary (graphical data from four patients). Activity due to the prior injection of RISHA was recorded and then subtracted before the renogram data were processed using a Varian computer. The computer displayed a diagram of the graph $\frac{R(\mathrm{t})}{B(\mathrm{t})}$ against $\int_0^t B(\mathrm{t})\mathrm{dt}/B(\mathrm{t})$ similar to the upper right part of Fig. 1. This enabled an operator to choose which points to use for analysis to obtain the best available straight line. The chosen points were then analysed to obtain F and K, and then $F.B(\mathrm{t})$ subtracted from the renogram data. The blood curve and corrected renogram were then smoothed and deconvoluted using an iterative technique, and finally Fig. 1 was printed out on a Statos plotter. The deconvolution value was calculated from the mean value of the second to fifth points on the deconvolution curve, divided by the time, T, between samples (20 seconds) *i.e.*, $DV=(D(2)+D(3)+D(4)+D(5))/80$.

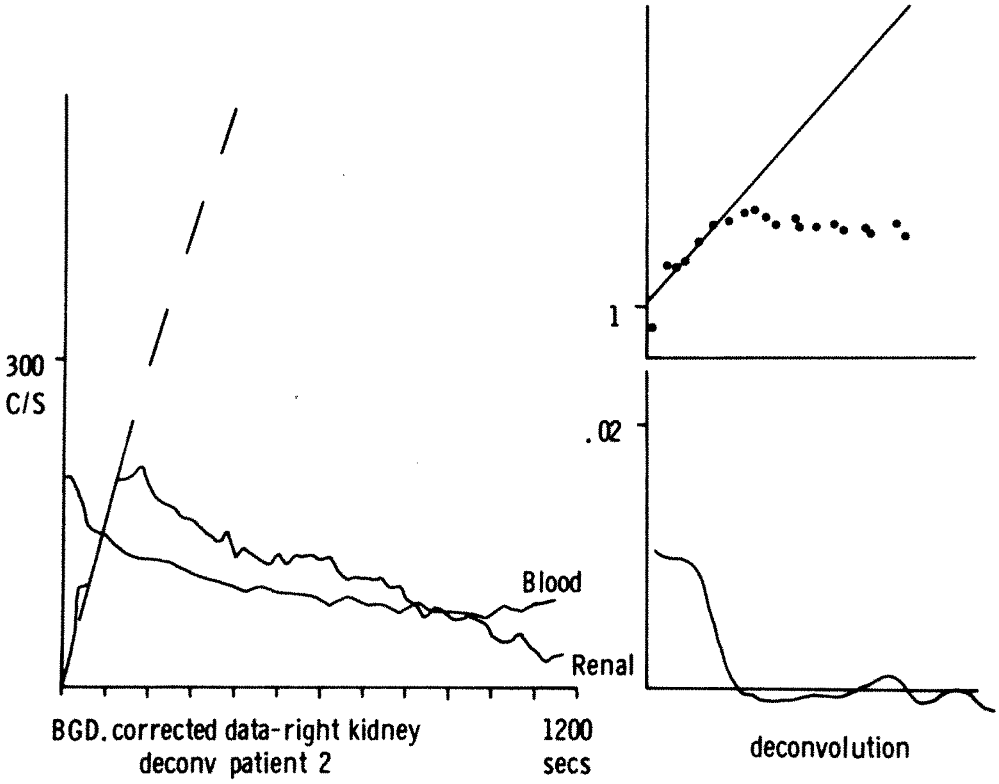

FIG. 1.

Left Section—Blood and background-corrected renal trace. The interrupted line is the integral of the blood curve multiplied by the uptake constant and represents the total material being taken up by the kidney. Up to 150 sec *i.e.*, it follows the corrected renogram until excretion begins.

Upper Right Section—The x-axis is SB/B and the y-axis R/B. It is the diagram from which points are chosen for analysis, in this particular case points 2 to 6. The line shown has the equation $Y=F+RK.X$.

Lower Right Section—Renal impulse response function H(t) obtained by deconvolution.

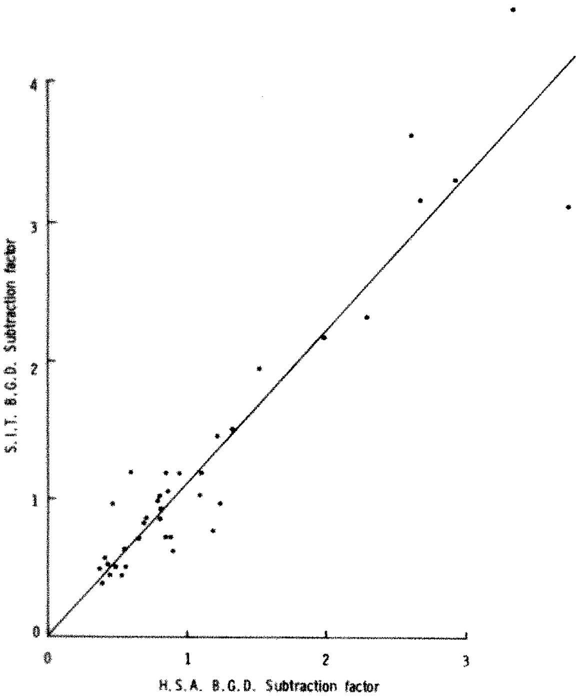

Fig. 2.

Regression of background subtraction factor by single injection technique against HSA technique. The line represents $y=0.02+1.11x$, $r^2=0.90$.

Results

Data from three patients were excluded. In one the background subtraction factor could not be determined after HSA injection due to a fault in the blood detector part of the system; in two other patients the hippuran appeared to have been given as an initial injection of 10% of the material, followed by the remaining material one to two minutes later. Data from all the other patients were used, and the results of analysis are presented in Figs. 1 and 2.

Regression analysis of the data gave the following results:

y = background subtraction factor by single injection technique

x = background subtraction factor from HSA

$y=0.0195+1.1089x$

$r^2=0.90$ (see Fig. 2)

y = deconvolution value

x = uptake constant

$y=0.0016+0.7744x$

$r^2=0.98$ (see Fig. 3).

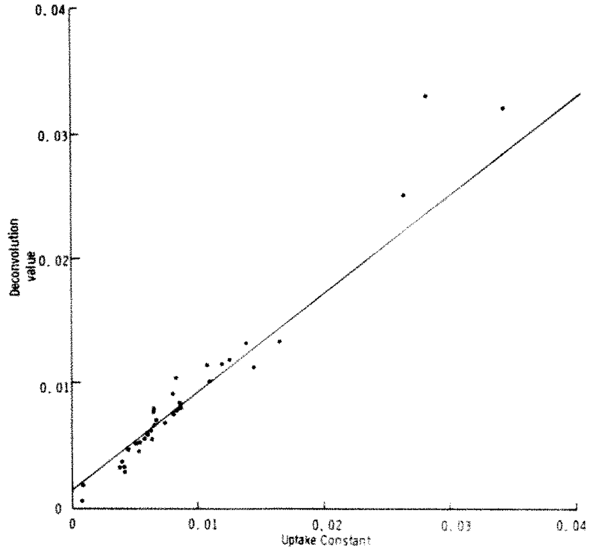

Fig. 3.

Regression of uptake constant by deconvolution against single injection technique. The line represents $y=0.0016+0.774$, $r^2=0.98$. 3 points off scale.

These results indicated a significant correlation between the blood-background subtraction factor obtained from RIHSA and that obtained from the single injection technique, and between the uptake constant and the deconvolution value.

Discussion

The method of analysis described is at present used with a Varian computer system, but was originally developed on a programmable calculator. The ratio of uptake constants provides an index of relative renal function between right and left kidneys.

The SIT analysis produces blood-background subtraction factors 11% higher than those obtained by RIHSA. The RIHSA method is considered to produce a subtraction factor 5–7% too small (Britton and Brown 1971) so the single injection method can be considered to produce results 5% above the "true value" which, for probe renography, is within acceptable limits.

There is a greater difference between the uptake constant and the deconvolution value (theoretically the same), but with several potential causes. The uptake constant is derived from unsmoothed data and points between 40 and 160 seconds, whilst the deconvolution value is derived from smoothed data between 40 and 100 seconds. Further analysis of data from 12 of the patients, taking the deconvolution value as the average of the third to fifth points (60–100 sec) and using less smoothing, changed the ratio of deconvolution value:uptake constant from 0.77 to 0.95.

This method of blood-background subtraction is not necessarily confined to renography, and the theory is applicable to any physiological system in which a tracer is absorbed from the blood and retained by an organ for a significant time.

ACKNOWLEDGMENTS

I should like to thank R. Barber and P. Crossland for help and advice with the computer, and N. J. G. Brown, Middlesex Hospital, London and R. Lawson, Manchester Royal Infirmary, for lending me the data for analysis. In addition, I am grateful to Dr. E. P. Wraight for constructive criticism, and I wish to thank Mrs. Thorburn from the Department of Medical Illustration, Addenbrooke's Hospital, for preparation and photography of the graphs.

REFERENCES

BRITTON, K. and BROWN, N. J. G., 1971. *Clinical Renography* (Lloyd-Luke, London).

DIFFEY, B. L., HALL, F. M., and CORFIELD, J. R., 1976. The $^{99}Tc^{m}$-DTPA Dynamic renal scan with deconvolution analysis. *Journal of Nuclear Medicine, 17*, 352–355.

KENNY, R. W., ACKERY, D. M., FLEMING, J. S., GODDARD, B. A., and GRANT, R. W., 1975. Deconvolution analysis of the scintillation camera renogram. *British Journal of Radiology, 48*, 481–486.

REEVE, J., CRAWLEY, J. C. W., HAMILTON, S. M., and GOLDBERG, A. D., 1975. Deconvolution analysis of the standard renogram and its clinical application. *Proceedings of the III International Symposium of Radionuclides in Nephrology*, 321–325.

REEVE, J. and CRAWLEY, J. C. W., 1974. Quantitative radioisotope renography: the derivation of physiological data by deconvolution analysis using a single injection technique. *Clinical Science and Molecular Medicine, 47*, 317–330.

Book review

Radiologic exploration of impotence. By J. F. Ginestié and A. Romieu, pp. 135, 80 figs., 1978. (Martinus Nijhoff Medical Division, The Hague/Boston/London). 50 Guilders. ISBN 90-247-2023-0.

The authors of this monograph from Montpellier are a radiologist and a sexologist. Their work is based on experience "with 250 patients whose examinations included 460 arteriograms of the internal iliac artery and 52 roentgenograms of the cavernous bodies". They conclude that one out of every four patients has impotence of vascular origin (p. 133). When patients are properly selected for arteriography, 93% of examinations show abnormal findings (p. 112). These are made up of mainly distal (perineal) lesions in younger men ("an infectious factor is often found" p. 89), and of diffuse lesions in older men. These are all illustrated in detail, but aortic bifurcation and common iliac artery disease is expressly excluded from the discussion (p. 65)—it is not clear to me why.

The book has many fine selective arteriograms of the internal iliac arterial tree, annotated with diagrams. These add up to an interesting atlas of normal anatomy and abnormal findings in individual patients. I missed guidance on the exact prevalence and importance of the various lesions described, and on their impact on patient management. There are a few paragraphs on "therapeutic perspectives" (p. 111) which say predictable things about sexual pathology as a "pathology of relationship", but not about what difference the arteriogram has made. The work is therefore strong on individual case description, but weak on convincing lessons.

The translator is anonymous, and this is just as well. The language of the book is far from current usage. This can amount to amusement over inventions like vascular "re-permeabilization" (p.71), but easily swings over to embarrassment ("this monograph purports to study" p. 13) and plain muddle: on p. 21 the best catheter tip is described "to penetrate the internal iliac artery"—just what the authors do not want to do. And what of captions like: "Patient 40 year old man. Brutal onset of impotence after a brucellien prostatsis" (sic on p. 105)? The printers contribute their share of trouble, like printing an explanatory diagram upside down *and* left-to-right reversed (p. 95). The authors have been very poorly served.

This is an interesting collection of individual cases for the new specialty of andrology. I doubt whether it will find a wider audience outside this small circle.

THOMAS SHERWOOD

1979, *British Journal of Radiology*, *52*, 138–144

Blood flow clearance changes in pig skin after single doses of X rays

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ABSTRACT

Early and late changes in the functional vascularity of pig skin have been evaluated after X-irradiation. These changes were assessed using a quantitative isotopic clearance technique. Two waves of radiation-induced changes in isotopic clearance were demonstrated. The first wave, observed after an interval of three weeks, was characterized by the faster clearance of the tracer from areas of irradiated skin. The second wave, which reached a peak after 12 weeks, was denoted by a slowing of the clearance rate relative to normal skin. The modification in vascular function observed at 12 weeks was transient, function returning to normal as late radiation damage developed. The changes observed in the pig have many similarities with those recorded in man but are markedly different from those found in rodents. These differences are discussed with respect to the vascular structure of the skin of the animal species investigated.

In the treatment of cancer by radiotherapy, the skin and deeper vascular connective tissues are of necessity nearly always included in any treatment field. Damage to these tissues is often dose limiting in effecting the local control of malignant disease. For this reason and because radiation reactions in the skin are so readily observable, this tissue has been used for the study of both the acute and late effects of ionizing radiation. Such investigations have been undertaken in rodents (Field, 1969; Moulder *et al.*, 1975), pigs (Archambeau *et al.*, 1968; Withers *et al.*, 1978; Hopewell *et al.*, 1978a) and man (Bates, 1975; Brennan *et al.*, 1976). Pig skin which has the same gross appearance as human skin (Montagna and Yun, 1964; Berry *et al.*, 1974) has in addition many histological similarities (Daniel and Williams, 1973; Donovan, 1975) and as such it is perhaps the most appropriate model using laboratory animals. In particular, late radiation changes, relevant to those observed in patients, have only been observed in the pig (Hopewell *et al.*, 1979).

Several of these reports of gross and histological changes in the skin after irradiation have suggested that damage to the vascular system plays an important role in the pathogenesis of late damage (Rubin and Casarett, 1968; Tessmer, 1971). Measurements of the overall efficiency of the local circulation, by investigating the regional blood flow, would appear to be a useful parameter for studying the circulatory status of a tissue after exposure to X rays.

Blood flow measurements in skin have been shown to be of great value in the study of plastic and reconstructive surgery (Barren *et al.*, 1951) and in the investigation of skin diseases (Aschheim, 1965). Very few studies have, however, been documented as to the effects of ionizing radiation on the vascular system of the skin after exposure to therapeutic doses (Roswit *et al.*, 1953; Glatstein, 1973; de Ruiter and van Putten, 1975).

Of the various methods available for the measurement of dermal blood flow, those utilizing radioisotopes have been shown to be the most reproducible and are most readily quantified (Kety, 1948; 1949). An isotopic clearance technique has been evaluated in pig skin (Moustafa and Hopewell, 1977; Young and Hopewell, 1979) using the tracer technetium 99m as the pertechnetate ion. The same technique has been used here to study quantitatively the effects of X irradiation on the functional vascularity of pig skin. Single doses which have previously been shown (Berry *et al.*, 1974; Hopewell *et al.*, 1978b) to produce radiation changes above and below "tolerance" have been used.

MATERIALS AND METHODS

Female pigs of the English Large White strain were used in these investigations. Animals were admitted to the Institute when they were about 12 weeks old (20 kg). They were allowed a period of two weeks to adapt to their new environment before any experimental procedures were performed. All experiments were carried out under general anaesthesia as described previously (Berry *et al.*, 1974).

Prior to irradiation, two to four standard fields measuring 16 × 4 cm were tattooed with indian ink on each flank of the pig. Fields were separated from each other by a 4 cm gap (Patterson, 1968). For each animal, fields on the left flank were irradiated while those on the right flank acted as controls in subsequent studies. The skin fields to be irradiated were delimited by a Perspex-ended applicator and a 16 × 4 cm cut-out in 3 mm lead placed over the skin. Single doses of 800, 1800, 2070 and 2340 rad were delivered to groups of 6 to 12 skin fields at 68 rad/minute from a 250 kV X-ray unit operating at 15 mA with 0.5 mm

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Reprint requests to J. W. Hopewell.

copper and 1.0 mm aluminium added filtration (HVL 1.3 mm Cu).

Measurements of isotope clearance rate were carried out simultaneously in irradiated and control sites after the intradermal injection of the tracer, $^{99}Tc^{m}$ as the pertechnetate ion (1–2 mCi/ml). The possible effects of isotope volume on the clearance rate of the tracer from the injection site was tested by the use of a small (0.03 ml) or medium (0.07 ml) volume of the tracer. The clearance of the tracer from the injection sites was monitored by two matched NaI crystal detectors connected to a multichannel analyser (Nokia LP 4840) which provided a digital record of changes in count-rate with time. The resultant clearance curves have a bi-exponential form; the two components are represented by the half clearance times derived from the two slopes (Moustafa and Hopewell, 1976; Moustafa, 1977). One component is referred to as the fast and the other the slow exponent and they are denoted by half-clearance times t_2 and t_1 respectively.

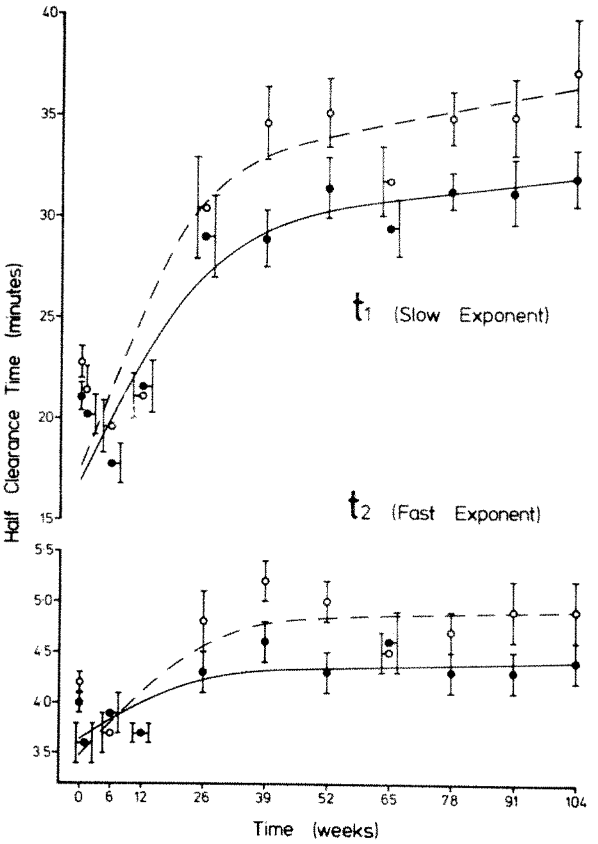

FIG. 1.

Half clearance times for the fast (t_2) and the slow (t_1) exponents of isotope clearance from a site of intradermal injection in pig skin, plotted against the age of the animals. Time zero represents 3–3.5 month old animals. Results obtained following the use of a small (O - - - O) and a medium (●—●) tracer volume are given.

RESULTS

In areas of normal pig skin on the animals used in the irradiation study, changes were noted in the clearance parameters with increasing age (Fig. 1). For the slow exponent the half clearance time (t_1) was found to increase significantly over the period 12–39 weeks after the initiation of measurements; it then remained relatively stable. The fast exponent (t_2), on the other hand, showed only marginal

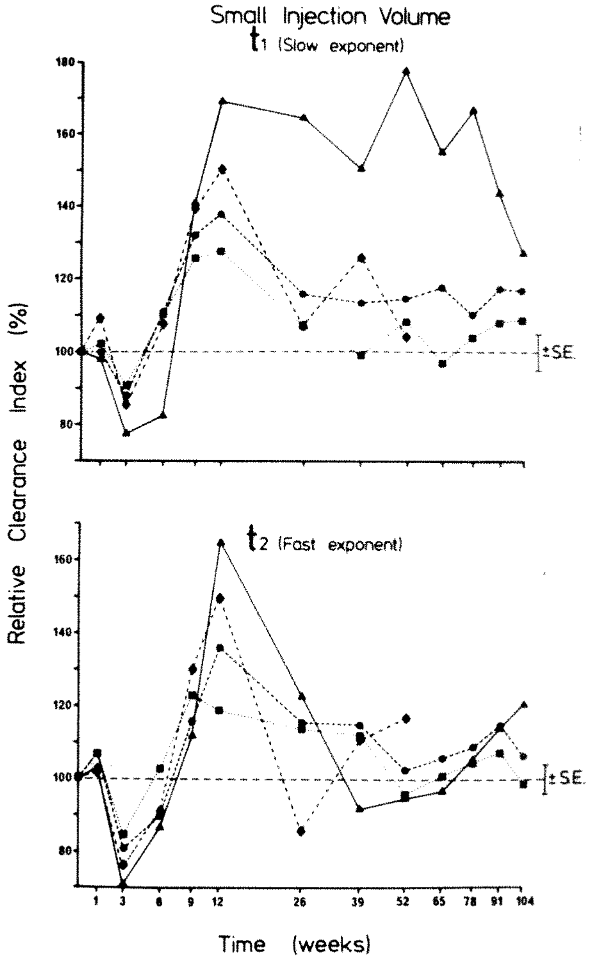

FIG. 2.

Time and dose related changes in the relative clearance index for the fast (t_2) and slow (t_1) exponents of isotope clearance after the intradermal injection of a small volume of tracer into pig skin (±S.E.—standard error of the mean for pretreatment values in normal pig skin) ■. . . ■ 800 rad; ●- - - ● 1800 rad; ◆-.-.-◆ 2070 rad; ▲——▲ 2340 rad).

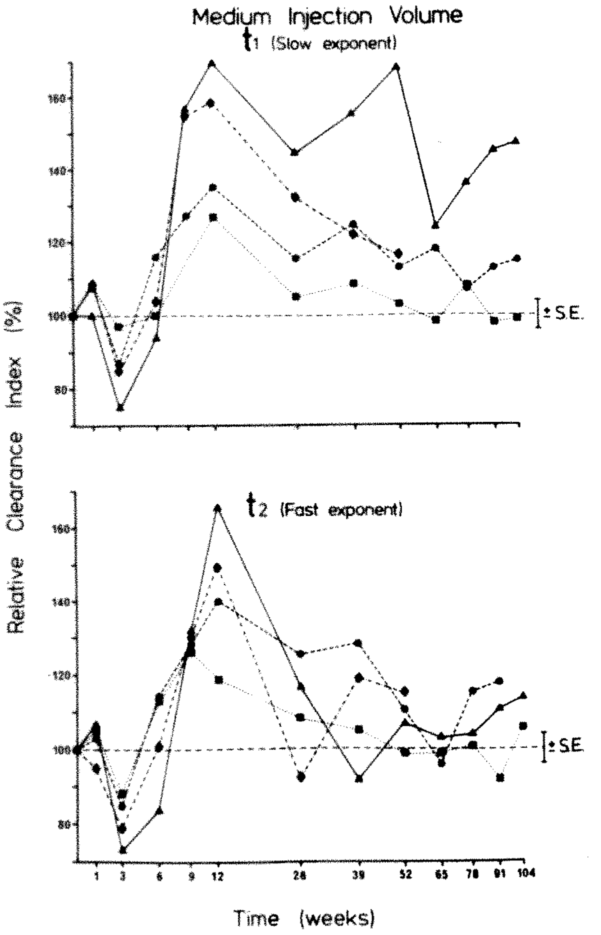

Fig. 3.

Time and dose related changes in the relative clearance index for the fast (t_2) and slow (t_1) exponents of isotope clearance after the intradermal injection of a medium volume of tracer into pig skin (key as in Fig. 2).

changes during the period of study. In young animals the volume of tracer injected did not influence the half clearance values obtained. However, in adult pigs the numerical values tended to be smaller after the injection of a medium volume of tracer, although these differences were only occasionally significant.

In the irradiation studies the half clearance times for both the fast (t_2) and slow (t_1) exponents of isotope clearance were compared with measurements in normal skin obtained at the same time. The ratio of irradiated to normal half clearance times is referred to as the relative clearance index. Examination of the variation in relative clearance index with time after irradiation showed two periods of major modification in the rate of isotope clearance from irradiated skin (Figs. 2 and 3).

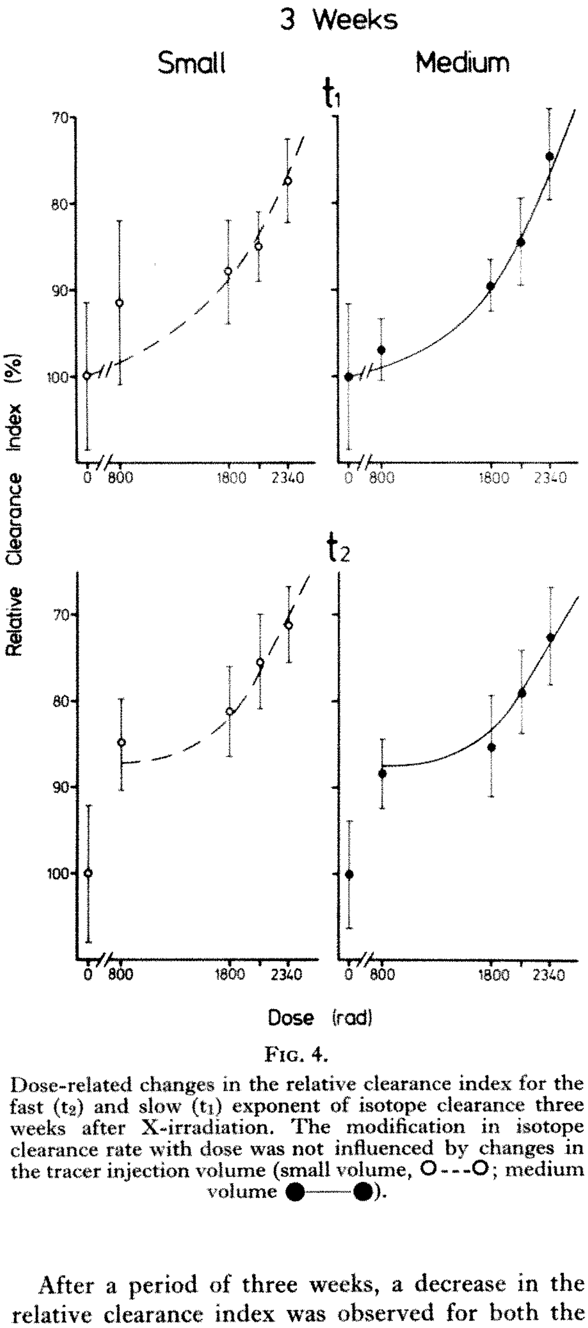

Fig. 4.

Dose-related changes in the relative clearance index for the fast (t_2) and slow (t_1) exponent of isotope clearance three weeks after X-irradiation. The modification in isotope clearance rate with dose was not influenced by changes in the tracer injection volume (small volume, ○---○; medium volume ●——●).

After a period of three weeks, a decrease in the relative clearance index was observed for both the fast (t_2) and the slow (t_1) exponents, *i.e.* the half clearance times obtained from measurements in irradiated skin were shorter than those found in normal skin. At twelve weeks the reverse was true, areas of irradiated skin taking much longer to clear isotope from the site of injection than normal skin. The two exponents of isotope clearance were not modified by increasing the tracer injection volume from 0.03 to 0.07 ml (Figs. 2 and 3).

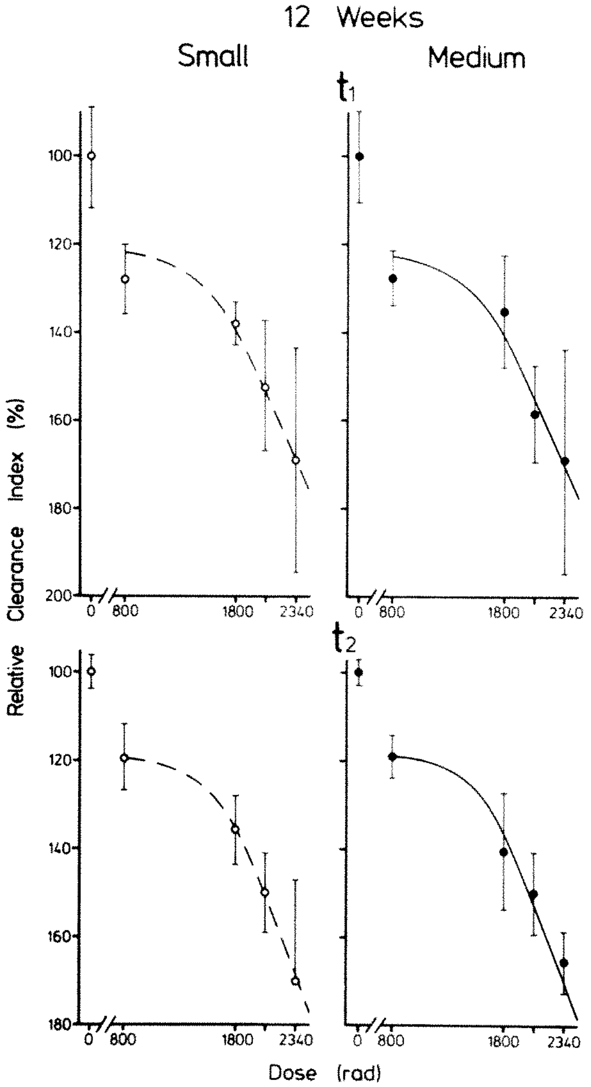

FIG. 5.

Dose-related changes in the relative clearance index for the fast (t_2) and slow (t_1) exponent of isotope clearance 12 weeks after X-irradiation. The modification in isotope clearance rate with dose was not influenced by changes in the tracer injection volume (small volume, O - - - O; medium volume ●——●).

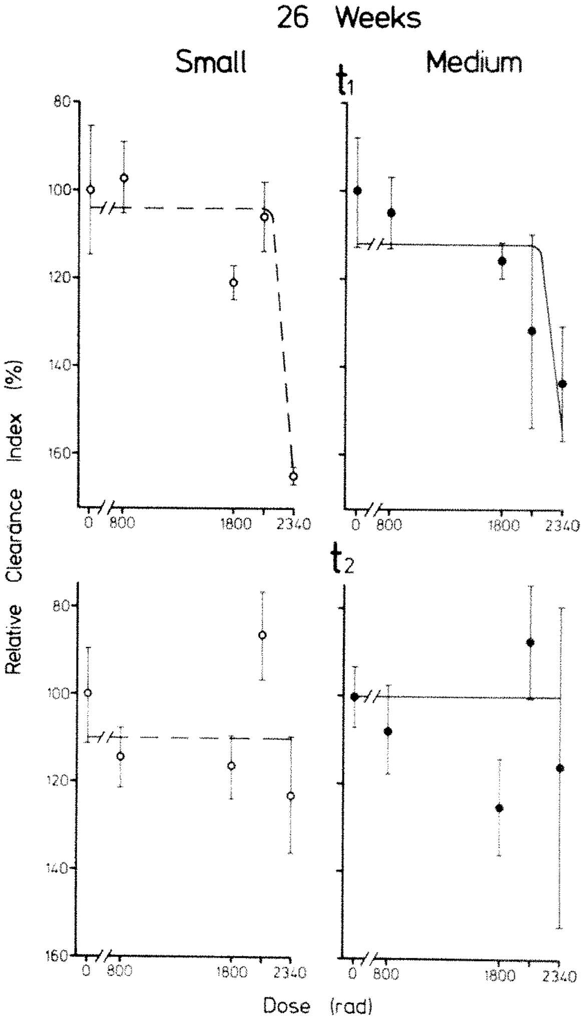

FIG. 6.

Absence of dose-related changes in the relative clearance index for the fast (t_2) and slow (t_1) exponent of isotope clearance 26 weeks after X-irradiation (small tracer volume O - - - O; medium tracer volume ●——●).

The modifications in isotope clearance from irradiated pig skin at three and 12 weeks after irradiation were dose dependent after an initial shoulder (Figs. 4 and 5). These changes in relative isotope clearance rates could be interpreted as an initial increase in net dermal blood flow after three weeks followed by a net reduction in flow per unit volume of tissue after a period of 12 weeks.

An initial plateau region of 0.5 to 15 minutes was found in a proportion of the clearance curves obtained from areas of skin nine and 12 weeks after irradiation. This plateau region indicates a delay in the commencement of clearance of the tracer from the site of injection. A total of 40% of skin areas receiving the two highest doses (2070–2340 rad) had a plateau or shoulder region at the beginning of the clearance curves. Shorter shoulder regions were also present in 19% of the fields treated with 1800 rad but they were not found in any of the fields treated with 800 rad.

The modifications in isotope clearance observed 12 weeks after irradiation with doses of 2070 and 2340 rad were associated with or preceded the development of areas of dermal necrosis (Berry *et al.*, 1974; Hand *et al.*, 1979). Most of these areas of necrosis healed quickly although in others there was persistent ulceration. Areas of skin associated with previous necrosis were avoided in any subsequent clearance studies.

The modification in isotope clearance observed after 12 weeks was transient, the relative clearance gradually returning to normal in the subsequent months (Fig. 6). The improvement in clearance rate in irradiated skin is not as large as it would appear, because of the changes in the value of the half clearance times found in normal skin over the same time period (Fig. 1). Only in areas of skin treated with the highest dose, 2340 rad, was the improvement in the relative clearance index in irradiated skin apparently delayed and this only applied to the slow exponent (Figs. 2 and 3). The significance of this finding is, however, difficult to evaluate, because only two fields on a single pig were available for investigation over the period 26–104 weeks, other fields being lost as a result of dermal necrosis. This disparity in results for the slow exponent (t_1) is further explained by the unusually low half clearance times obtained for normal skin on this animal. At six months mean values of 18.9 and 17.0 minutes were obtained for the small and medium injection volumes as compared with the respective overall mean values of 30.4 and 29.0 minutes (Fig. 1). The half clearance values obtained for the associated irradiated areas of skin on this pig were comparable with these overall mean values for normal skin. For all the other treatment doses the clearance rate was similar to normal over the period 26–104 weeks after irradiation, irrespective of whether a small or medium tracer injection volume was used (Figs. 2 and 6).

Discussion

The modification in isotope clearance rate in normal pig skin with increasing age might reflect a reduction in metabolic activity in mature animals. Kety (1948, 1949) originally assumed that the method measured nutritional blood flow. This suggestion is supported by the report (Brody and Kibler, 1944) that the resting metabolism of growing animals is greater than that of mature ones. Female swine reach a metabolic peak at about seven months of age, after which they decline, reaching a plateau when they are fourteen months old. In the present study isotope clearance rates remained stable in animals aged 14–24 months. Aging of the microvasculature may also be a factor. The density of blood vessels in the reticular dermis of pig skin has also been found to decline with age (Young and Hopewell, 1979). Slower clearance rates have also been observed in human skin with increasing age (Braithwaite *et al.*, 1951; Buchanan *et al.*, 1954) but not in rats (Keyeux *et al.*, 1971).

The two waves of response in the modifications of isotope clearance from irradiated pig skin in the first six months after X-irradiation is in keeping with the gross changes observed. Two distinct waves of erythema have been reported in the first few months after treatment (Berry *et al.*, 1974; Hand *et al.*, 1979; Hopewell *et al.*, 1978a; Turesson, 1978). Two waves of reaction have also been noted as a result of a systematic thermographic study on radiotherapy patients (Martin—personal communication). The initial rise and the subsequent fall in skin temperature he observed could be interpreted as an increase followed by a decrease in dermal blood flow.

The rapid rate of isotope clearance observed three weeks after irradiation is probably related to a vasodilatation of the fine vasculature and/or a change in vascular permeability, as an early response to radiation. Similar changes have been reported as the erythema reaction develops in radiotherapy patients (Roswit *et al.*, 1953; White *et al.*, 1975) and human volunteers after ultra-violet irradiation (Levan *et al.*, 1964). Direct histological evidence of vasodilatation as an early reponse to radiation has been reported in mouse skin (Takahashi and Kallman, 1977). This was denoted by an increase in vascular diameter and vascular volume four weeks after irradiation with single doses of 2000 and 4000 rad. An increase in vascular permeability has been reported in irradiated rabbit skin, this reaching a maximum 23 days after treatment (Jolles *et al.*, 1961; Eassa-Helmy and Casarett, 1973).

No early change in blood flow has been demonstrated in rodent skin (Glatstein, 1973; Keyeux *et al.*, 1971) with doses up to 2000 rad. This might be related to the considerable differences in vascular structure in rodent skin as compared with human and pig skin (Donovan, 1975).

The early changes in isotope clearance reported in pig and human skin are associated with and may be a direct result of radiation damage to the basal cells of the epidermis. The suggested link between early changes in vascular permeability to fibrinogen and late damage in rodents (Law and Thomlinson, 1978) would seem to be unfounded because of the lack of correlation between initial epidermal damage and late effects (Hopewell *et al.*, 1979; Arcangeli *et al.*, 1974; Turesson, 1978).

The most distinct change seen in irradiated pig skin after three months was characterized by the significant lengthening of the clearance rate of the tracer from treated areas. This is thought to be related to an impairment of the vascular system due to direct radiation damage to blood vessels or to a reduction in their net function. Evidence of vascular occlusive changes (Hopewell *et al.*, 1978a) and a reduction in vascular density (Young and Hopewell, unpublished data) have been demonstrated in the pig dermis. Similar reductions in vascular length and vascular surface area have also been observed in rodent skin (Takahashi and Kallman, 1977) 12 weeks after irradiation.

In addition one might suggest that there is a relationship between the initial delay in the clearance of the tracer, observed at nine and 12 weeks after irradiation, and the severe oedema noted at the same time period; the high tissue pressure results in a transient vascular collapse which produces the plateau region on the clearance curves. The reduction in blood flow and the oedema seem likely to contribute to the eventual breakdown of the dermis. In areas of irradiated skin not associated with dermal necrosis the isotope clearance rate gradually returns to normal.

The isotope clearance technique used essentially measures clearance per unit volume of tissue. The return of the clearance parameters to normal could occur as a result of parenchymal atrophy or be explained in part by revascularization. Recent preliminary quantitative histological studies (Young *et al.*, unpublished data) have shown a similar vascular density in atrophied irradiated and normal skin in 1–2 year old pigs. Functional studies have provided a similar result in areas of human skin showing evidence of late radiation damage (Roswit *et al.*, 1953; Wiernik and Patterson, 1977).

In contrast to pig and man a late decrease in the blood flow clearance rate has been observed in rodent skin (Keyeux *et al.*, 1971; de Ruiter and van Putten, 1975). This change occurred 11–12 months after irradiation with doses of 2000 to 3000 rad.

The good correlation between the modification of isotope clearance reported in the present study and late linear field contraction (Hopewell *et al.*, 1978a, 1979) is consistent with the view that this transient impairment in vascularity is responsible for the development of late damage in pig skin. Evidence that transient vascular changes are important in the development of late effects have been reported in lung (Moustafa and Hopewell, 1977; Glatstein, 1973), brain (Moustafa, 1977; Moustafa and Hopewell, 1979; Hopewell *et al.*, 1978b), the hamster cheek pouch (Hopewell and Young, 1978), spleen and bone marrow (Nelson *et al.*, 1974; 1977). These changes are observed between two and nine months after irradiation with single doses of 1500–3000 rad.

Thus in summary there are a number of observations recorded in the present study, using normal and irradiated pig skin, which correlate well with changes noted in human skin. Most of these changes are markedly different from results obtained in rodent skin. Both early and late functional changes observed in irradiated pig skin show a good correlation with reported morphological changes. While similar morphological changes have been noted in rodent skin one must speculate that the absence of functional changes is related to the different vascular structure of the dermis in the two species. The greater vascularity of rodent skin makes it less sensitive to the consequences of irradiation damage. The similarities in response between human and pig skin would support the view that this should be the animal of choice in this field of clinically orientated radiobiological research.

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REFERENCES

ARCANGELI, G., FRIEDMAN, M. and PAOLUZI, R., 1974. A quantitative study of late radiation effects in normal skin and subcutaneous tissues in human beings. *British Journal of Radiology*, *47*, 44–50.

ARCHAMBEAU, J. O., MATHIEU, G. R., BRENNEIS, H. J., THOMPSON, K. H. and FRIARCHILD, R. G., 1968. The response of the skin of swine to increasing single exposures of 250 kVp X rays. *Radiation Research*, *36*, 299–326.

ASCHHEIM, E., 1965. Clearance of NaI^{131} from normal and edematous skin. *Journal of Investigative Dermatology*, *44*, 141–143.

BARRON, J. N., VEALL, N. and ARNOTT, D. G., 1951. The measurement of the local clearance of radioactive sodium in tubed skin pedicles. *British Journal of Plastic Surgery*, *4*, 16–27.

BATES, T. D., 1975. A prospective clinical trial of post-operative radiotherapy delivered in three fractions per week versus two fractions per week in breast carcinoma. *Clinical Radiology*, *26*, 297–304.

BERRY, R. J., WIERNIK, G. and PATTERSON, T. J. S., 1974. Skin tolerance to fractionated X-irradiation in the pig—how good a predictor is the NSD formula? *British Journal of Radiology*, *47*, 185–190.

BRAITHWAITE, F., FARMER, F. T. and HERBERT, F. I., 1951. Observations on the vascular channels of tubed pedicles using radioactive sodium. *British Journal of Plastic Surgery*, *4*, 38–47.

Brennan, D., Young, C. M. A., Hopewell, J. W. and Wiernik, G., 1976. The effects of varied numbers of dose fractions on the tolerance of normal human skin. *Clinical Radiology*, *27*, 27–32.

Brody, S. and Kibler, H. H., 1944. LIX. Resting energy metabolism and pulmonary ventilation in growing swine. *Ministry of Agriculture Experimental Stations Research Bulletin*, *380*, 1–20.

Buchanan, T. J., Walls, E. W. and Williams, E. S., 1954. Studies in radiosodium clearance from the skin in man. *Clinical Science*, *13*, 333–343.

Daniel, R. K. and Williams, H., 1973. The free transfer of skin flaps by microvascular anastomoses. An experimental study and a reappraisal. Part I: The vascular supply of the skin. *Plastic and Reconstructive Surgery*, *52*, 16–31.

Donovan, W. E., 1975. Experimental models in skin flap research. In: *Skin Flaps*, Edited by Grabb, W. C. and Myers, M. B. (Little, Brown and Company, Boston), 11–20.

Eassa-Helmy, M. E. and Casarett, G. W., 1973. Effects of epsilon-amino-n-caproic acid (EACA) on radiation-induced increase in capillary permeability. *Radiology*, *106*, 679–688.

Field, S. B., 1969. Early and late reactions in skin of rats following irradiation with X-rays or fast neutrons. *Radiology*, *92*, 381–384.

Glatstein, E., 1973. Alterations in rubidium-86 extraction in normal mouse tissues after irradiation. An estimate of long-term blood flow changes in kidney, lung, liver, skin and muscle. *Radiation Research*, *53*, 88–101.

Hand, J. W., Field, S. B., Hopewell, J. W. and Foster, J. L., 1979. The response of pig skin to combined X-irradiation and microwave heating. *Radioscience*, (In press.)

Hopewell J. W., Foster, J. L., Gunn, Y., Moustafa, H. F., Patterson, T. J. S., Wiernik, G. and Young, C. M. A., 1978a. The role of vascular damage in the development of late radiation effects in the skin. In: *Late Biological Effects of Ionizing Radiation*. I.A.E.A. Vienna, 1, 483–492.

Hopewell, J. W., Foster, J. L., Young, C. M. A. and Wiernik, G., 1979. Late radiation damage to pig skin: the effects of overall treatment time and number of fractions. *Radiology*, (in press).

Hopewell, J. W., Reinhold, H. S., Wilkinson, J. and Blackeivicz, B., 1978b .Changes in the architecture of blood vessels of the rat brain after local irradiation. (Abstract). *British Journal of Radiology*, *51*, 561.

Hopewell, J. W. and Young, C. M. A., 1978. Changes in the microcirculation of normal tissues after irradiation. *International Journal of Radiation Oncology, Biology, Physics*, *4*, 53–58.

Jolles, B., Remington, M. and Simon-Reuss, I., 1961. Indirect radiation effects and diffusible factors in irradiated tissues (stromatex). *Acta Radiologica*, *56*, 57–64.

Kety, S. S., 1948. Quantitative measurement of regional circulation by the clearance of radioactive sodium. *American Journal of Medical Science*, *215*, 352–353.

1949. Measurement of regional circulation by the local clearance of radioactive sodium. *American Heart Journal*, *38*, 321–328.

Keyeux, A., Dunjic, A., Royer, E., Jovanovic, D. and Van de Merckt, J., 1971. Late functional and circulatory changes in rats after local irradiation. *International Journal of Radiation Biology*, *20*, 7–25.

Law, M. P. and Thomlinson, R. H., 1978. Vascular permeability in the ear of rats after X-irradiation. *British Journal of Radiology*, *51*, 895–904.

Levan, N. E., Hyman, C., Freedman, R. and Rohter, F., 1964. Biphasic changes in cutaneous effective blood flow after ultra-violet irradiation. *Journal of Investigative Dermatology*, *43*, 451–452.

Montagna, W. and Yun, J. S., 1964. The skin of the domestic pig. *Journal of Investigative Dermatology*, *43*, 11–21.

Moulder, J. E., Fischer, J. J. and Casey, A., 1975. Dose-time relationship for skin reactions and structural damage to rat feet exposed to 250 kVp X rays. *Radiology*, *115*, 465–470.

Moustafa, H. F., 1977. The use of radioisotopic techniques to demonstrate early and late vascular changes in irradiated tissues. D.Phil. thesis, University of Oxford.

Moustafa, H. F. and Hopewell, J. W., 1976. The evaluation of an isotopic clearance technique for the measurement of skin blood flow in the pig. *Microvascular Research*, *11*, 147–153.

1977. Measurement of lung function in the pig after local X-irradiation. In *Radiobiological Research and Radiotherapy*, *IAEA*, *Vienna*, *1*, 75–83.

1979. Effects of local irradiation on the functional vascularity of the rat brain (unpublished).

Nelson, D. F., Chaffey, J. T. and Hellman, S., 1974. The long-term effects of X-irradiation on the ability of the spleen to support clonegenic proliferation. *Radiation Research*, 58, 417–431.

1977. Late effects of X-irradiation on the ability of mouse bone marrow to support hematopoiesis. *International Journal of Radiation Oncology, Biology, Physics*, *2*, 39–45.

Patterson, T. J. S., 1968. The survival of skin flaps in the pig. *British Journal of Plastic Surgery*, *21*, 113–117.

Roswit, B., Wisham, L. H. and Sorrentino, J., 1953. The circulation of radiation damaged skin. Radiosodium clearance studies. *American Journal of Roentgenology*, *69*, 980–990.

Rubin, P. and Casarett, G. W., 1968. *Clinical Radiation Pathology*. Volumes 1 and 2. (W. B. Saunders & Company, Philadelphia).

de Ruiter, J. and van Putten, L. M., 1975. Measurement of blood flow in the mouse tail after irradiation. *Radiation Research*, *61*, 427–438.

Takahashi, M. and Kallman, R. F., 1977. Quantitative estimation of histological changes in the subcutaneous vasculature of the mouse after X-irradiation. *International Journal of Radiation Oncology, Biology, Physics*, *2*, 61–68.

Tessmer, C. F., 1971. Radiation effects in skin. In: *Pathology of Irradiation* (Ed. Berdjis, C. C.), (Williams & Wilkins Company, Baltimore), 146–170.

Turesson, I., 1978. Fractionation and dose rate in radiotherapy. Ph.D Thesis, University of Goteborg, Sweden.

White, R. L., El-Mahdi, A. M. and Ramirez, H. L., 1975. Thermographic changes following preoperative radiotherapy in head and neck cancer. *Radiology*, *117*, 469–471.

Wiernik, G. and Patterson, T. J. S., 1977. Blood flow measurements in irradiated grafts and normal skin of patients. *9th European Conference of Microcirculation*, *(Antwerp) Bibliotheca Anatomica*, *15*, 331–336 (Karger, Basel).

Withers, H. R., Thames, H. D., Flow, B. L., Mason, K. A. and Hussey, D. H., 1978. The relationship of acute to late skin injury in 2 and 5 fraction week γ-ray therapy. *International Journal of Radiation Oncology, Biology, Physics*, *4*, 595–601.

Young, C. M. A. and Hopewell, J. W., 1979. Evaluation of an isotope clearance technique in pig skin: correlation of functional and histological changes (unpublished).

1979, *British Journal of Radiology*, *52*, 145–147

Technical note

Selenium 75 contamination in iodine 131 solutions

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During investigations on athyreotic patients given large test doses of ^{131}I, whole-body counting has shown the presence of ^{75}Se contamination in some patients. The investigations were carried out to measure the small long-term component of ^{131}I retention in such patients. In an earlier paper (Smith and Edmonds, 1977), we concluded that the effects of ^{75}Se contamination were negligible in the patients described. Subsequent studies on a further small group of similar patients, however, have indicated that the levels of contamination are variable, and this report is intended as a warning of the possibility of measurement error due to this contamination in metabolic studies similar to those to be described. The effects of ^{75}Se contamination observed in two out of five patients studied have been assessed.

METHODS

Whole-body counting measurements, using the CRC multi-crystal (NaI) counter, were made on five female patients who had previously undergone total thyroidectomy followed by radioiodine therapy for the treatment of thyroid carcinoma, and in whom there was no further evidence of residual ^{131}I-concentrating tissue. The patients were given a test dose (5 mCi) of ^{131}I, at University College Hospital, as part of routine follow-up procedure and two whole-body retention measurements were made about 10 and 20 days after the dose. Two measurements were sufficient to determine the half-life of the long-term component of ^{131}I retention, which has previously been shown to follow a single exponential (Edmonds *et al.*, 1970; Smith and Edmonds, 1977). Immediately after the second measurement, a calibrating dose of about 1 μCi ^{131}I was administered orally, followed 1 hour later by a final measurement. On all occasions, whole-body γ-ray spectra were obtained using a 128 channel analyser. Counts were integrated in two ^{131}I channels, I_1 (0.31–0.41 MeV) and I_2 (0.58–0.70 MeV), and in the ^{75}Se channel, S_1 (0.1–0.31 MeV). Crossover ratios were determined to correct the counts in I_1 for those due to ^{75}Se and to correct for the effects of ^{131}I in S_1. The corrected counts in I_1 (the main ^{131}I peak) were used to determine the half-time of the ^{131}I retention component, and the counts in I_2, which are unaffected by ^{75}Se, were used as a check on this value. The corrected counts in S_1 were used to estimate the amount of ^{75}Se present on each occasion. ^{131}I crossover in channel S_1 was obtained using whole-body ^{131}I spectra from patients who contained no ^{75}Se, since the net γ-ray spectrum measured only 1 hour after the ^{131}I calibrating dose was unsuitable for this purpose. Similarly, ^{75}Se crossover was obtained using spectra from patients in a different study measured several days after administration of ^{75}Se-seleno methionine.

RESULTS

The whole-body γ-ray spectra from two of the five patients showed clear evidence of contamination with small amounts of ^{75}Se although they had not been given ^{75}Se per se at any time before these measurements. The spectra from one of these patients are shown in Fig. 1 and those from one of the other three patients are shown in Fig. 2. Net spectra resulting from ^{131}I calibration doses (normalized to 1 μCi ^{131}I) are also shown. In both patients contaminated with ^{75}Se, the ratio of retained ^{75}Se to ^{131}I was higher at the time of the second whole-body measurement. In Table I the number of counts in channel I_1 due to ^{131}I and ^{75}Se are given separately and the biological half-life of ^{131}I has been calculated before and after correction for ^{75}Se to indicate the extent of the error incurred if the ^{75}Se contamination had not been recognized and allowed for. The corrected values for the biological half-life of ^{131}I are in good agreement with those calculated using channel I_2, although the accuracies of the latter are limited by low count rates. Table II shows the estimated whole-body content of ^{75}Se in the two contaminated patients at each measurement.

DISCUSSION

Contamination of ^{131}I solutions (from The Radiochemical Centre, Amersham) with ^{75}Se, probably present as selenite, results from trace quantities of

TABLE I

WHOLE-BODY RETENTION OF ^{131}I AND ^{75}SE CONTAMINANT IN TWO ATHYREOTIC PATIENTS GIVEN TEST DOSES OF 5 mCi ^{131}I

	1st measurement				2nd measurement				T_b of ^{131}I (days)		
		I_1 (counts s^{-1})				I_1 (counts s^{-1})			I_1		
Patient	Day	^{131}I	^{75}Se	I_2 (counts s^{-1})	Day	^{131}I	^{75}Se	I_2 (counts s^{-1})	uncorrected*	corrected	I_2
1	12	271.0	4.3	18.4	22	85.3	2.9	5.8	25.3	23.7	23.9
2	11	325.4	9.2	22.1	20	108.7	7.7	7.4	22.4	19.6	19.7

T_b = biological half-life.
I_1 = counting channel (0.31 – 0.41 MeV) for main ^{131}I photopeak.
I_2 = counting channel (0.58 – 0.70 MeV) for high energy ^{131}I photopeak.
*Uncorrected for ^{75}Se contamination.

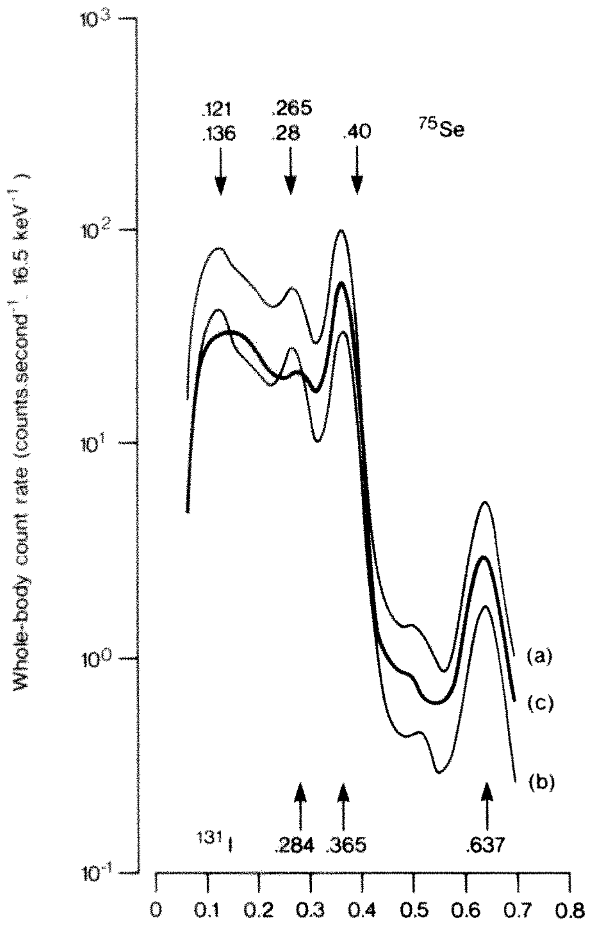

FIG. 1.

Whole-body γ-ray spectra from athyreotic patient given a test-dose of 5 mCi ^{131}I, showing presence of ^{75}Se contamination. Spectra were measured 11 days (A) and 20 days (B) after the dose. The net spectrum measured 1 h after a calibrating dose of 1 μCi ^{131}I is shown (C).

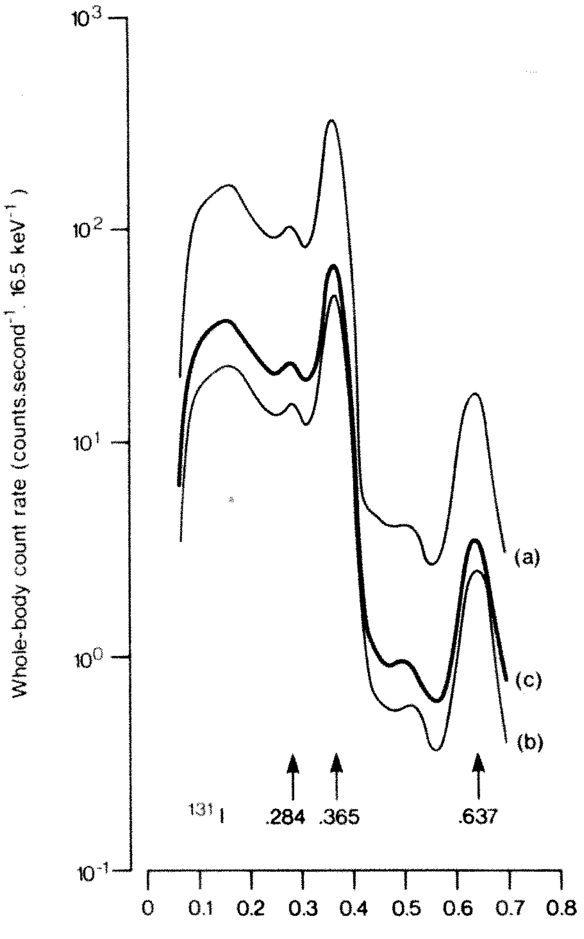

FIG. 2.

Whole-body γ-ray spectra from athyreotic patient given a test dose of 5 mCi ^{131}I, showing no evidence of ^{75}Se contamination. Spectra were measured 8 days (A) and 22 days (B) after the dose. The net spectrum measured 1 h after a calibrating dose of 1 μCi ^{131}I is shown (C).

TABLE II
LEVELS OF WHOLE-BODY ^{75}SE CONTAMINATION IN TWO ATHYREOTIC PATIENTS GIVEN TEST DOSES OF 5 mCi ^{131}I

Patient	1st measurement		2nd measurement	
	Day	^{75}Se (μCi)	Day	^{75} Se(μCi)
1	12	0.19	22	0.13
2	11	0.46	20	0.38

selenium impurities in the tellurium dioxide target material used for ^{131}I production. At the ^{131}I activity reference date, the contamination is less than 0.02% (*i.e.* <200 nCi ^{75}Se per mCi ^{131}I) which is the manufacturer's limit of detectability, and is thus not observed at the time of administration of ^{131}I. In patients without a thyroid, however, more than 99% of administered ^{131}I is excreted rapidly as iodide with half-life of about 0.5 day (Pochin, 1964), followed by a very small component ($\sim$0.2%) of organically bound ^{131}I which is eliminated with an effective half-life of about 5 days (Smith and Edmonds, 1977). The relative proportion of ^{75}Se in the body, which is more slowly excreted, thus rises progressively, becoming detectable within a few days. Effective half-lives of between 40 and 65 days have been observed for about 75% of an initial body content of ^{75}Se-selenite (Cavalieri *et al.*, 1966; Thomson and Stewart, 1974). Measurement errors may thus arise because the highest energy γ ray of ^{75}Se (0.40 MeV) cannot be resolved from the main ^{131}I γ ray (0.36 MeV) using NaI detectors.

Only two patients out of five had detectable contamination with ^{75}Se. They had all received ^{131}I doses at different times and possibly ^{75}Se contamination in different batches of ^{131}I is variable. Some variation may be explained by the length of time in stock before each ^{131}I dose is administered and this should be as short as possible.

As shown in Table I, the effect of the presence of ^{75}Se in the more contaminated patient (No. 2) would have been to increase the estimated biological half-life of ^{131}I to 22.4 days from the corrected value of 19.6 days. A larger error would have resulted if a longer period between the two whole-body retention measurements had been chosen. The estimated level of ^{75}Se contamination in this patient was about 0.46 μCi, 11 days after an oral dose of 5 mCi ^{131}I. From published data on whole-body retention of ^{75}Se-selenite in man (Cavalieri *et al.*, 1966; Thomson and Stewart, 1974), it can be estimated that the initial absorption by this patient would have been about 0.6 μCi, resulting from an intake of about 1 μCi ^{75}Se (0.02% of the ^{131}I activity given). It is possible that the two contaminated patients were given their ^{131}I doses later than the ^{131}I reference date.

In radioiodine treatment of thyroid carcinoma, therapeutic doses of 150 mCi ^{131}I are administered to thyroidectomized patients. If ^{75}Se contamination was present at the level of the limit of detectability (0.02% of ^{131}I activity), 30 μCi of ^{75}Se-selenite would be given with each dose. It can be estimated that about 20 μCi of the ^{75}Se would be absorbed (Thomson and Stewart, 1974) and would deliver a whole-body radiation dose of about 0.13 rad (Jereb *et al.*, 1975). Thus, despite the longer effective half life of the ^{75}Se contaminant, the radiation dose it delivers to the whole body is negligible in relation to that due to the ^{131}I (Pochin, 1967).

We have also observed ^{75}Se contamination in thyroidectomized pigs given several large doses of ^{131}I within the space of a few months in studies similar to those described above. Tissues recovered at the end of the studies contained variable levels of ^{75}Se contamination. The highest concentration (nCi kg^{-1}) was observed in kidney, being twice that in spleen and five times that in liver.

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REFERENCES

CAVALIERI, R. R., SCOTT, K. G., and SAIRENJI, E., 1966. Selenite (^{75}Se) as a tumour-localizing agent in man. *Journal of Nuclear Medicine*, *7*, 197–208.

EDMONDS, C. J., SMITH, T., and BARNABY, C. F., 1970. Follow-up of thyroid carcinoma by whole-body counting. *British Journal of Radiology*, *43*, 868–875.

JEREB, M., FALK, R., JEREB, B., and LINDHE, C., 1975. Radiation dose to the human body from intravenously administered ^{75}Se-sodium selenite. *Journal of Nuclear Medicine*, *16*, 846–850.

POCHIN, E. E., 1964. Formulation of relationships between the radiation exposure of tissues and the excretion rate of nuclides. In: *Assessment of Radioactivity in Man* (Proceedings of the Symposium on Assessment of Radioactive Body Burdens in Man, Heidelberg, May 11–16, 1964), Vol. 1, pp. 3–14 (International Atomic Energy Agency, Vienna).

POCHIN, E. E., 1967. Prospects from the treatment of thyroid carcinoma with radioiodine. *Clinical Radiology*, *18*, 113–125.

SMITH, T., and EDMONDS, C. J., 1977. A slow component of iodine turnover in athyreotic individuals. *Clinical Science and Molecular Medicine*, *53*, 81–86.

THOMSON, C. D., and STEWART, R. D. H., 1974. The metabolism of [^{75}Se] selenite in young women. *British Journal of Nutrition*, *32*, 47–57.

1979, *British Journal of Radiology*, *52*, 148–149

Case reports

Cystic lymphangioma of the spleen: a cause of splenomegaly

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(*Received May, 1978*)

Expansive lesions of the spleen are rare, especially true cysts and primary tumours, and very seldom are diagnosed prior to operation (Tuttle and Minielly, 1978). Angiography has been the best method for making the diagnosis and to evaluate splenic involvement by tumours (Ekelund *et al.*, 1975).

Recently we have examined a patient with splenomegaly which was due to a cystic lymphangioma. Only two previous angiographic reports of this entity are available (Shanser *et al.*, 1973; Tuttle and Minielly, 1978) and only three cases have been described.

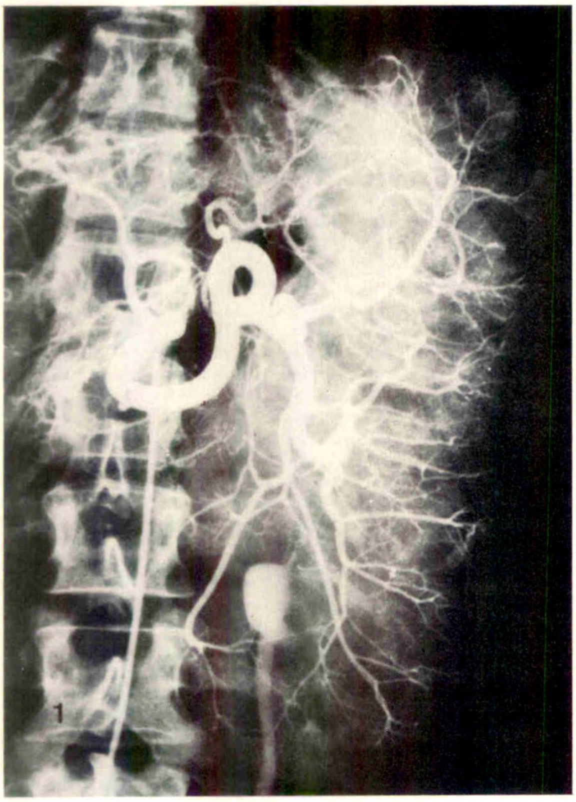

FIG. 1.

Early phase of splenic artery angiography shows splenomegaly with stretched intraparenchymatous arteries displaced around avascular areas.

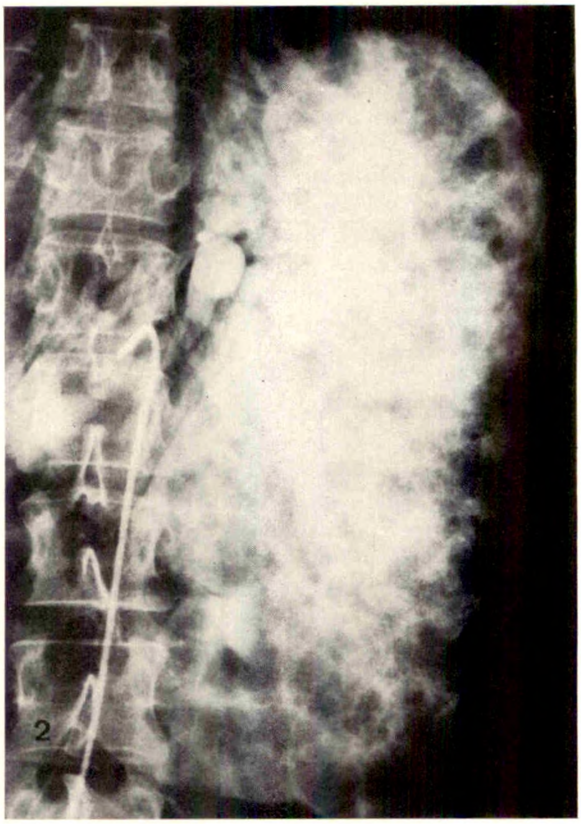

FIG. 2.

Late phase angiogram shows the "swiss cheese" like appearance of the multiple avascular defects of the spleen.

CASE REPORT

A 31-year-old white woman was admitted to this hospital with diarrhoea, loss of weight and anorexia for two months. Physical examination was normal except for a massively enlarged spleen, which extended to the mid-line. Laboratory studies, including complete blood count, sedimentation rate and chest bone biopsy were all normal.

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Selective angiography of the splenic artery confirmed the splenomegaly and showed that the entire spleen was involved with stretched intraparenchymatous arteries displaced around avascular areas. No encasement or tumour vessels were seen (Fig. 1). The late phase of the angiogram disclosed irregular contrast accumulation with multiple avascular defects throughout the spleen (Fig. 2).

The patient underwent splenectomy and recovery was uneventful. The specimen consisted of the spleen which weighed 1.300 g and showed a "swiss cheese" appearance with multiple small cysts containing watery fluid. Flattened endothelial cells lined the cysts. The diagnosis of cystic lymphangioma of the spleen was made.

DISCUSSION

The signs and symptoms of lymphangioma of the spleen are not distinctive and only splenomegaly is evident. The true incidence is not known and authors are unable to indicate the aetiology (McClure and Altemeier, 1942).

Few cases of lymphangiomatous cysts of the spleen have been angiographically examined. According to the literature the angiographic pattern is characteristic. The present case showed the same widespread arterial changes and avascular defects which have been described previously (Shanser *et al.*, 1973; Tuttle and Minielly, 1978). From now this entity should be considered in the differential diagnosis of splenomegaly.

Only angiography can disclose the nature of splenic enlargement and show the changes of cystic lymphangioma of the spleen, allowing the correct pre-operative diagnosis.

ACKNOWLEDGMENTS

We wish to thank Prof. Trygve Aakhus for his kind permission to use this case from his department.

REFERENCES

EKELUND, L., GÖTHLIN, J., and PETTERSSON, H., 1975. Angiography in expansile lesions of the spleen. *Acta Radiologica*, *125*, 81–90.

MCCLURE, R. D., and ALTEMEIER, W. A., 1942. Cysts of the spleen. *Annals of Surgery*, *116*, 98–102.

SHANSER, J. D., MOSS, A. A., and CLARCK, R. E., 1973. Angiographic evaluation of cystic lesions of the spleen. *American Journal of Roentgenology*, *119*, 166–174.

TUTTLE, R. J., and MINIELLY, J. A., 1978. Splenic cystic lymphangiomatosis: an unusual cause of splenomegaly. *Radiology*, *126*, 47–48.

The build up of technetium in breast milk following the administration of $^{99}Tc^{m}O_4$ labelled macroaggregated albumin

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When $^{99}Tc^{m}O_4$ labelled macroaggregated albumin is administered to a lactating mother it may be necessary to delay the resumption of feeding. This can cause various problems including the discomfort experienced by the mother and a possible reaction by the child. The practice in Aberdeen, in the few cases experienced, has been to recommend a delay of 36 hours following an administered dose of 500 μCi before feeding is resumed.

In a recent review article (Anderson, 1977) on drugs and breast feeding it was suggested that it would be safe to resume feeding after 24 hours. The work quoted (Berke *et al.*, 1971) dealt with a dose administered to a mother who had been feeding her child for six months.

CASE REPORT

This paper concerns a mother who was referred for a lung scan almost immediately following the birth of her child. The mother wished to start feeding the child soon after the scan as she had successfully fed her two previous children. As this case was unusual in that feeding had not yet commenced and the mother was willing to co-operate, it was decided to monitor the build up and fall of technetium in expressed samples, firstly of colostrum and later of milk. These data could then be compared with those of Berke and the suitability of the 24 hour delay checked.

Starting two hours after the injection of 500μCi at 16.00 h, samples were expressed at four hourly intervals except during the period 22.00 h to 06.00 h. These were counted

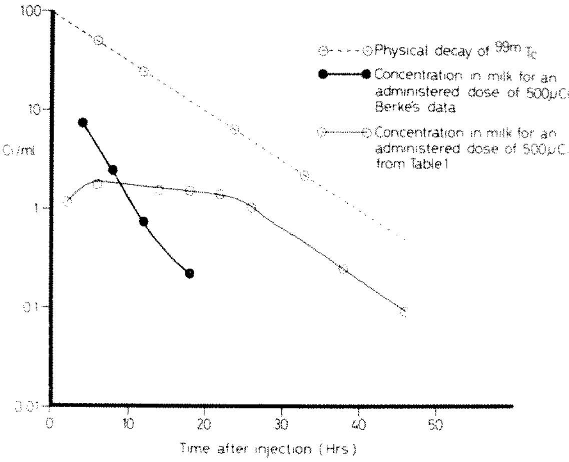

FIG. 1.

Comparison of activity concentration in expressed milk samples.

1979, *British Journal of Radiology*, *52*, 150–152

TABLE I

ACTIVITIES OF EXPRESSED SAMPLES

Sample No.	Breast	Vol., ml.	Collection time after injection, hours	Count in 1200 sec corrected to time of collection	Activity, nCi/ml.
1	Right	3	2	6.54×10^4	1.16
2	Left	2	2	6.19×10^4	
3	Right	1	6	4.44×10^4	1.74
4	Left	1.75	6	6.04×10^4	
5	Right	0.75	14	2.78×10^4	1.60
6	Left	0.75	14	2.48×10^4	
7	Right	5	18	1.89×10^5	1.57
8	Left	4	18	1.21×10^5	
9	Both	7	22	2.16×10^5	1.40
10	Both	8	26	1.90×10^5	1.09
11	Both	3.8	38	2.1×10^4	0.25
12	Right	20	46	4.08×10^4	0.09
13	Left	20	46	3.85×10^4	

Background: 760 counts in 1200 sec.

and the count rates adjusted to the count rate at the time of collection. Variation in efficiency due to counting samples of different volume were also accommodated. Using a standard, the activities of the samples were then calculated. Our results are compared with those of Berke (adjusted to an administered dose of 500μCi) in Fig. 1. The results are given in Table I.

DISCUSSION

The large initial difference in the two sets of data is probably due to different rates of breakdown of the macroaggregate. In that used by Berke, breakdown could have been so rapid that the maximum output occurred sometime before the first sample at four hours, whereas in our case technetium was apparently being made available for some 20 hours after the injection. Further work is now being undertaken to check this. There is also a difference in the type of sample collected over the first 20 hours following the injection. The samples collected by Berke were full milk samples. Those collected in Aberdeen were at first nearly all colostrum and it was not until about 20 hours following the injection that the milk content started to rise.

Despite the large differences in output noted above, the conclusion drawn by Berke that feeding could be resumed 24 hours after the injection is still valid and will be adopted in future. If this procedure is followed the whole-body dose to the baby would be something less than 0.05 millirem and that to the thyroid some 20 times higher. The dose to the baby due to its close proximity to the mother in the period following the injection would be larger but still only a few millirem.

REFERENCES

ANDERSON, P., 1977. Drugs and breast feeding—a review. *Drug Intelligence and Clinical Pharamcology, 11*, 208–223.

BERKE, R. A., HOOPS, E. C., KEREIAKES, J. C., and SAENGER, E. L., 1971. Radiation dose to breast feeding child after mother had ^{99m}Tc-MAA lung scan. *Journal of Nuclear Medicine, 14*, 51–52.

Demonstration of a patent porta-caval anastomosis by ultrasound

By K. C. Dewbury, B.Sc., F.R.C.R., and A. E. A. Joseph, M.Sc., F.R.C.R.

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The portal venous system is almost always visualized in ultrasound images of the upper abdomen. In portal hypertension the increased diameter of the portal vein may be measured on ultrasound images (Doust and Pearce, 1976). This measurement may be of value both in diagnosis and follow-up of patients. In portal vein thrombosis the normal vascular anatomy at the porta hepatis is replaced by a broad band of high level echoes. The appearance is characteristic (Webb *et al.*, 1977). A case is presented

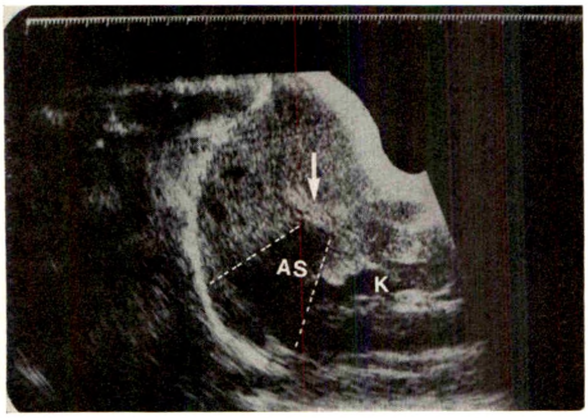

FIG. 1A.

Longitudinal section through the right lobe of the liver showing the presence of high amplitude echoes at the porta hepatis (arrowed) and the absence of a normal portal vein. The high amplitude echoes cast an acoustic shadow (AS). K = Kidney.

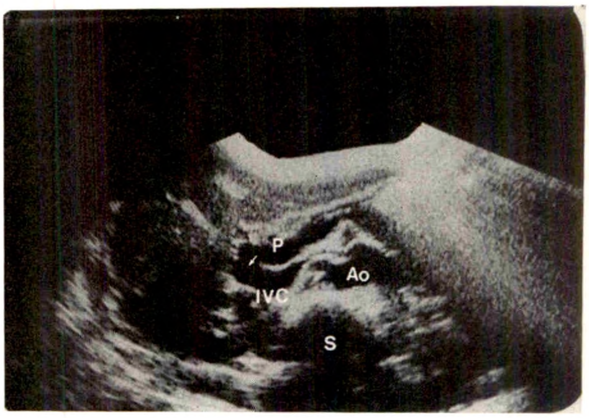

FIG. 2A.

Transverse section at the level of the splenic and portal veins (P). The portal vein is clearly seen running into the inferior vena cava (IVC). Ao = Aorta. S = Spine.

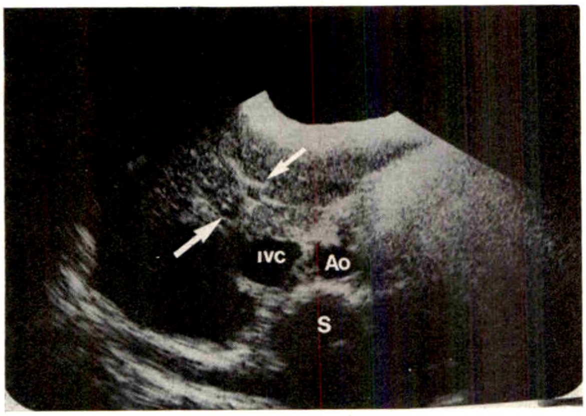

FIG. 1B.

Transverse section showing the porta hepatis (arrowed). A band of high amplitude echoes replaces the normal portal vein. Within this region small transonic areas represent recanalization. IVC = Inferior vena cava. Ao = Aorta. S = Spine.

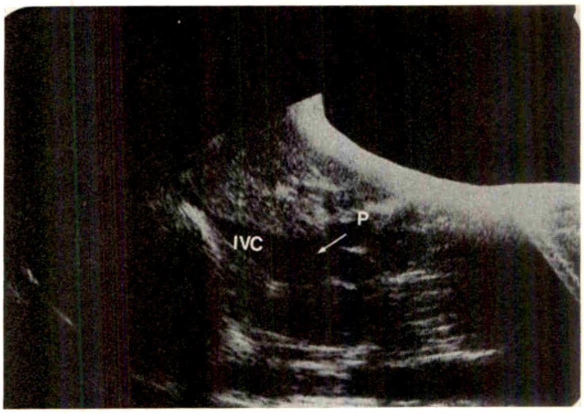

FIG. 2B.

Longitudinal scan along the inferior vena cava (IVC) showing the portal vein (P) connecting with the anterior wall of the IVC.

showing the findings of portal vein thrombosis and a porta-caval anastomosis. The patency of the anstomosis was demonstrated on the ultrasound images.

CASE HISTORY

A 42-year-old male with a past history of liver disease was admitted for assessment of his liver function prior to aortic valve replacement for Grade II aortic incompetence.

At the age of 18 he presented with a haematemesis from oesophageal varices. These were shown to be secondary to cirrhosis. A lieno-renal anastomosis was performed, followed two years later by oesophagogastrectomy. Four years later (1960), following further bleeding, a porta-caval anastomosis was performed. At the time of the present admission the patient had no symptoms referable to his liver. An ultrasound examination was performed as part of the liver assessment. The ultrasound images show the characteristic findings of portal vein thrombosis with a band of high amplitude echoes at the porta hepatis indicating surrounding fibrosis. Within this region irregular transonic areas are seen representing partial recanalization or venous collaterals (Figs 1A and 1B). The splenic vein and the proximal part of the portal vein are clearly demonstrated. The latter is enlarged, measuring 17 mm at its maximum diameter. The inferior vena cava is also seen and is large. On both longitudinal and transverse sections the dilated portal vein can be seen entering the inferior vena cava. Both vessels are patent (Figs. 2A and 2B).

COMMENT

Ultrasound is a quick and reliable method by which to assess the portal venous system and its patency, in particular to confirm or exclude portal vein thrombosis. This case illustrates its value as a means of assessing the patency of vascular shunts. One can speculate that in conjunction with pulsed doppler measurements, flow studies could also be carried out.

REFERENCES

DOUST, B. D. and PEARCE, J. D., 1976. Greyscale ultrasonic properties of the normal and inflamed pancreas. *Radiology*, 120, 653–657.

WEBB, L. J., BERGER, L. A., and SHERLOCK, S., 1977. Greyscale ultrasonography of the portal vein. *Lancet*, October, 675–677.

Book reviews

Encyclopaedia of Medical Radiology, Vol. 10, Part 2a. Roentgen Diagnosis of the Heart and Blood Vessels. By K. H. Bigalke *et al.*, pp. ix+503, illus., 1977 (Springer Verlag, Berlin, Heidelberg, New York) DM 384/$192.00

Volume 10, Part 2a, 'Roentgen Diagnosis of the Heart and Blood Vessels', in 'Encyclopedia of Medical Radiology' has now been published. This volume contains chapters on the pathology of cardiac valve defects and of endocarditis, with special reference to the morphology of mitral, aortic, tricuspid and pulmonary valve disease. There is also a very comprehensive section on the radiology of various valve diseases dealing with dominant stenosis, incompetence and combined lesions. The cardiomyopathies are dealt with in an extended review and there are also two separate sections on other forms of myocarditis. The final chapter deals with the pathological anatomy and the clinical and radiological manifestations of pericarditis.

As one would suspect from the title of this volume, it is an encyclopaedic text covering the field very extensively and comprehensively with a very valuable and full bibliography which is truly all-embracing and international. The authors have not only provided us with this excellent bibliography, but what is even more helpful there is a complete authors index in addition to the general index; this is a very helpful innovation of great value to research workers in the various fields covered in the text. One could, of course, find gaps here and there in the literature since it is quite impossible in producing a volume of this kind to really keep up to date, but this very minor omission should not detract from the general value of this book.

There is, however, one problem about the reproductions since as in most German textbooks X-ray films are printed as negatives; although their quality is very good and the pictures are informative to the English speaking readers this way of reproducing radiographs is unusual and may detract somewhat from their value.

As is to be expected, Springers have again produced a beautifully illustrated and printed text of the same high standard as all the other volumes in this Encyclopaedia of Medical Radiology.

R. E. STEINER

Basic science of nuclear medicine. By Roy P. Parker, Peter H. S. Smith and David M. Taylor, pp. x+374, illus., 1978 (Churchill Livingstone, Edinburgh), £8·50.

This book is intended to be a general introductory text for physicians, scientists, radiographers and technicians entering nuclear medicine and related fields. Based as it is on the scientific content of the University of London M.Sc. course in Nuclear Medicine, which itself has evolved over a period of years, it is not surprising to find that it achieves this objective admirably. The various sections cover the relevant topics in physics, instrumentation, data analysis, radiation biology, radiation dosimetry, basic chemistry and radiopharmaceutical preparation with a nice balance between theory and practice throughout. In a text which brings together so many widely differing specialized subjects it is exceedingly difficult to maintain a proper balance and to give the integrated picture which is all too often lacking in multi-author books. In the present case there can be no criticism on this score. Any reader who has already developed special interests in this field may well feel that his own particular topic is only covered superficially—for example the gamma camera gets but six pages—but he will then almost certainly find that the remaining chapters will fill a number of important gaps in his knowledge of related subjects, all of which are basic and therefore essential.

Those who are fortunate enough to have this text as their first introduction to the subject will be spared much of the anguish consequent upon the transition from classical to SI units. The clearly written chapter on radiation dosimetry, a notoriously difficult subject, is worthy of special mention. The new philosophy and concepts underlying the radiation protection recommendations in ICRP 26 are indicated, even though this particular document only became available in late 1977, implying extremely rapid publication. Perhaps this and the high quality of reproduction may have something to do with the book being printed in Singapore. In any event, it is not a publication for the library; anyone working in this field in whatever capacity will find a personal copy invaluable and the price does not rule this out.

N. VEALL

1979, *British Journal of Radiology*, *52*, 153–155

Short communication

Effect of dose rate on intestinal tolerance in mice. Implications in radiotherapy

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The effect of dose rate on intestinal tolerance after ^{60}Co γ-irradiation has been studied in BALB/c mice. Intestinal tolerance was assessed from LD50, after either selective abdominal irradiation or total-body irradiation.

Three dose rates were compared: 0.6 Gy/min ("acute irradiation" taken as reference), 0.05 Gy/min and 0.025 Gy/min.; the corresponding irradiation times were then about 20 min, 5 h and 12 h respectively. Irradiations were performed simultaneously, at these dose rates, with three telecobalt therapy units; the dose rates were adjusted with lead shields and by increasing the distances.

For abdominal irradiations the animals were immobilized with legs stretched by means of wooden clothes-pegs (Wambersie *et al.*, 1974). The immobilization times were the same (about 12 h) for all animals; they could bear it without anaesthesia.

After selective abdominal irradiation (a total number of 387 mice), LD50 at 5.5 days increased from 12.4 Gy to 20.2 Gy and 21.8 Gy when the dose rate decreased from 0.61 to 0.054 and 0.026 Gy/min respectively. The ratios of the LD50 ("acute irradiation" taken as reference) were then 1.6 and 1.8 respectively. For survival at 6.5 days, LD50 increased from 12.1 Gy to 19.2 Gy and 21.6 Gy respectively, and the corresponding LD50 ratios were then also 1.6 and 1.8 (Table I).

After total-body irradiation (a total number of 403 mice), LD50 at 5.5 days increased from 9.9 Gy to 15.2 Gy and 16.8 Gy, when the dose rate decreased from 0.56 to 0.049 and 0.024 Gy/min respectively. Although these LD50 values were somewhat lower than those observed after selective abdominal irradiation, their ratios were similar, *i.e.* 1.5 and 1.7 respectively (Table II).

This increase of LD50 as the dose rate decreases to 0.025 Gy/min is similar to the increase of LD50 observed, with the same strain of animals, in previous experiments with fractionated irradiations. In these previous experiments, LD50 was also increased by a factor of 1.8 when a single dose was replaced by a large number (at least 10) of small fractions (less than 2 Gy), the influence of proliferation being eliminated (Wambersie *et al.*, 1974).

Within both types of experiment, it can reasonably be assumed that LD50 corresponds to the same level of survival for the intestinal clonogenic cell population (Wambersie and Dutreix, 1974). It can also be assumed that this 1.8-fold increase of LD50 corresponds to full repair of sublethal damage. The maximum ratio may not have been reached with the lowest dose rate (0.025 Gy/min), but the exposure time could not be extended much longer than 12 h for technical reasons. However, the present results obtained with continuous low dose-rate irradiation were compatible with the two component model derived from multifraction experiments:

$$S = \left[e^{-D/{}_1D_0}\right]\left[1 - \left(1 - e^{-D/{}_nD_0}\right)^n\right]$$

with the following values of the parameters:
${}_1D_0 = 4.50$ Gy, ${}_nD_0 = 2.25$ Gy, $n = 10$ (Wambersie *et al.*, 1974).

From this model, iso-effect curves as a function of irradiation time were computed for different survival levels assuming random repair of the sublethal lesions (Dutreix and Sahatchiev, 1975). Present results are compatible with a half life, T, of 1.5 h (Fig. 1). Increase of the iso-effect dose with increasing irradiation time depends, in absolute and relative terms, on the survival level (or absorbed dose). In particular, the iso-effect dose should be nearly independent of dose rate for an absorbed dose of 2–3 Gy, for which cell lethality can be assumed to be caused mainly by direct lethal events.

The increase of LD50 observed, in the present experimental conditions, with decreasing dose rate is in rather good agreement with that expected from the above theoretical

TABLE I

Variation of LD50 for intestinal death as a function of absorbed dose rate
Selective abdominal irradiation with ^{60}Co in BALB/c mice

Absorbed dose rate (Gy/min)	Number of irradiated animals	Endpoint: survival at 5.5 days			Endpoint: survival at 6.5 days		
		LD50/Gy	Ratio	Irradiation time*	LD50/Gy	Ratio	Irradiation time*
0.61 (Reference)	236	12.4† (12.1–12.8)	1.00	20 min	12.1† (11.8–12.4)	1.00	20 min
0.054	76	20.2 (18.7–25.2)	1.6	6 h 14 min	19.2 (18.2–21.4)	1.6	5 h 56 min
0.026	75	21.8 (20.7–23.4)	1.8	13 h 58 min	21.6 (20.4–23.5)	1.8	13 h 50 min

*Calculated for LD50.
†Value of LD50 and between brackets 95% confidence interval.

TABLE II

VARIATION OF LD50 AT 5.5 DAYS FOR INTESTINAL DEATH AS A FUNCTION OF ABSORBED DOSE RATE
TOTAL BODY IRRADIATION WITH ^{60}Co IN BALB/c MICE

Absorbed dose rate (Gy/min)	Number of irradiated animals	Endpoint: survival at 5.5 days		
		LD50/Gy	Ratio	Irradiation time*
0.56 (Reference)	131	9.9† (9.6–10.3)	1.00	16 min
0.049	136	15.2 (14.3–16.1)	1.5	4 h 48 min
0.024	136	16.8 (16.0–17.7)	1.7	10 h 30 min

*Calculated for LD50.
†Value of LD50 and between brackets 95% confidence interval.

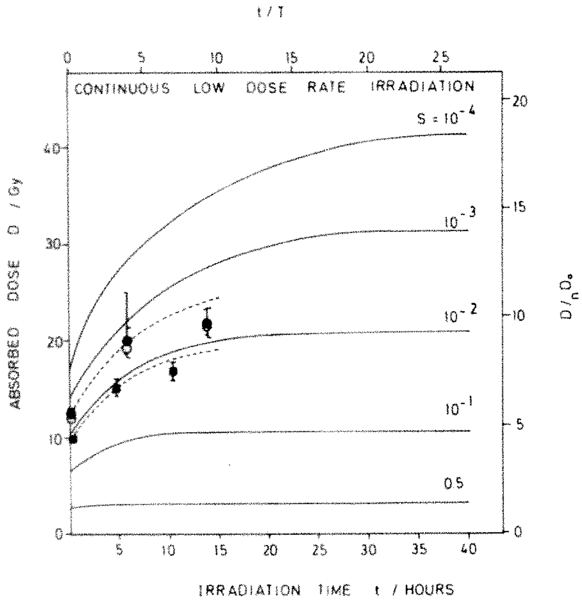

FIG. 1.

Iso-effect absorbed doses D corresponding to different survival levels S as a function of irradiation time t. The iso-effect curves are computed from the model with the values of the parameters given in the text.

Comparison with the present experimental points (circles, data from Table I; squares, data from Table II) indicates that the increase of LD50 observed with increasing irradiation time is in rather good agreement with that expected when considering only repair of sublethal lesions.

The ratio $D/_nD_0$ is presented in the right-hand ordinate, assuming $_nD_0 = 2.25$ Gy. The ratio t/T is presented in the upper abscissa, assuming $T = 1.5$ h.

model taking into account only repair of sublethal lesions (Fig. 1).

Finally, for animals surviving the intestinal syndrome after whole-body irradiation, LD50 scored at 30 days was not very different for the three dose rates (LD50/30 6–8 Gy). Although the number of animals was small (101 mice), this observation suggests that the bone-marrow syndrome is less dependent on dose rate, or irradiation time, than the gastrointestinal syndrome.

Comparison with the experimental data already published indicates that, for some biological systems and effects, the additional dose necessary to reach a given effect when passing from "acute" to "continuous low dose rate" irradiation is comparable to that expected when considering only repair of sublethal lesions (Kal, 1974; Kal and Sissingh, 1974). For other biological systems and effects, it is necessary to consider, besides repair of sublethal lesions, other mechanisms such as cell distribution (Frindel *et al.*, 1972; Kal, 1974) and, for tumours, the oxygen effect (Kal and Barendsen, 1972; Frindel *et al.*, 1972; Hill and Bush, 1973; Kal, 1974; Fu *et al.*, 1975).

A differential effect then appears to be possible (Pierquin *et al.*, 1975). However, as far as clinical applications are concerned, general agreement has not yet been reached on the exact shape of the iso-effect curves as a function of irradiation time for the effects relevant to radiation therapy (Paterson, 1963; Awwad *et al.*, 1974).

ACKNOWLEDGMENTS

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REFERENCES

AWWAD, H. K., BURGERS, J. M. V., and MARCUSE, H. R., 1974. The influence of tumour dose specification on the early clinical results of interstitial radium tongue implants. *Radiology*, *110*, 177–182.

DUTREIX, J. and SAHATCHIEV, A., 1975. Clinical radiobiology of low dose-rate radiotherapy. *British Journal of Radiology*, *48*, 846–850.

FRINDEL, E., HAHN, G. M., ROBAGLIA, D., and TUBIANA, M., 1972. Responses of bone marrow and tumour cells to acute and protracted irradiation. *Cancer Research*, *32*, 2096–2103.

FU, K. K., PHILLIPS, TH. L., KANE, L. J., and SMITH, V., 1975. Tumour and normal tissue response to irradiation. In vivo: variation with decreasing dose rates. *Radiology*, *114*, 709–716.

HILL, R. P. and BUSH, R. S., 1973. The effect of continuous or fractionated irradiation on a murine sarcoma. *British Journal of Radiology*, *46*, 167–174.

KAL, H. B., 1974. Responses of a rat and rhabdomyosarcoma rat skin to irradiation with gamma rays and 15 MeV neutrons at low dose rates. Doct. Thesis, University of

Amsterdam. Publ. of the Radiobiological Institute of the Organization for Health Research TNO, Rijswijk (Z-H), The Netherlands.

Kal, H. B. and Barensen, G. W., 1972. Effects of continuous irradiation at low dose-rates on a rat rhabdomyosarcoma. *British Journal of Radiology, 45*, 279–183.

Kal, H. B. and Sissingh, H. A., 1974. Effectiveness of continuous low dose-rate gamma-irradiation on rat skin. *British Journal of Radiology, 47*, 673–678.

Paterson, R., 1963. In *The Treatment of Malignant Disease by Radiotherapy*. 2nd Edition p. 210. (Edward Arnold, London).

Pierquin, B., Baillet, F., Mueller, W., and Wilson, F., 1975. Irradiation semi-continue à faible débit par télécobalt. *Journal de Radiologie et D'Electrologie, 57*, 841–843.

Wambersie, A., Dutreix, J., Gueulette, J., and Lellouch, J., 1974. Early recovery for intestinal stem cells, as a function of dose per fraction, evaluated by survival rate after fractionated irradiation of the abdomen of mice. *Radiation Research, 58*, 498–515.

Wambersie, A. and Dutreix, J., 1974. Cellular repair after X or gamma irradiation determined for several "gross" criteria on animals and patients. *European Journal of Cancer, 10*, 235–239.

Book reviews

Ultraschalldiagnostik (B-scan) in der inneren Medizin. Editor Harald Lutz. pp. xii+152, illus., 1978 (Springer Verlag KG, Berlin), D.M.78/$39.00.
ISBN 3-540-08189-5.

The value of this book is somewhat limited in the UK since the text is in German, and the equipment used for all examinations is the Vidoson, very few specimens of which are available within the UK. The main value of the book perhaps lies in its value as an indicator of the capability and limitations of real-time ultrasound examination of the abdomen.

The quality of the illustrations is very good, especially in terms of a grey-scale, but I found the line diagrams rather primitive although generally adequate. The book is essentially an atlas of illustrative cases and therefore contains a minimum of text. The number of references is rather larger than one would have expected in such a book and I found them extremely valuable. This book is also rather better than previous publications using illustrations from the same equipment, since in this atlas the orientation of all images has been standardized.

Much of the pathology shown is rather gross and examples of smaller masses within the liver would have been useful. The sections on thyroid and heart were particularly poor, though considering the limitations of the equipment the section on pancreas was unusually good. I was, however, somewhat surprised to note that in acute pancreatitis the author does not appear to note reduction in echoamplitudes as is seen by all other workers in this field. Conversely, carcinoma of the pancreas appears to display unusually low echoamplitudes and I wonder to what extent this is dependant upon patient selection or the type of equipment used.

The section on intestinal lesions is of dubious value especially since the author does not give a differential diagnosis for most of the examples shown.

On the whole the text is, however, fairly good, the author emphasizing the non-specific nature of the ultrasound findings in many conditions.

This book is unlikely to be useful to investigators wishing to examine patients with a conventional "B" scanner, and will, therefore, have only a very limited market in the UK

H. B. Meire.

Cross-Sectional Anatomy—an Atlas for Computerized Tomography. By Robert S. Ledley, H. K. Huang and John C. Maziotta, pp. xii+317, illus. (Williams & Wilkins Co., Baltimore), $69.95.

As computed tomography becomes more widely practised, there is a growing need for a comprehensive atlas demonstrating cross-sectional anatomy, as shown in the CT scan. This book relates anatomical diagrams to the CT image throughout the body including the limbs. Each double page includes a radiograph depicting the level of the cross-section which is an excellent idea, as well as diagrams in the sagittal and cross-sectional planes. Some of these cross-sectional diagrams are a little difficult to intepret, as all the structures, excluding muscle and bone, are represented by single line drawings without shading. The CT scans are illustrated both in colour and as a gray scale image. The colour illustrations seem to add little useful information. The quality of the CT scans is not as high as images produced by the majority of scanners currently available. In many examples it is difficult to define structures which should be clearly visible with CT. This is unfortunate but understandable because any book produced during the first three years of a rapidly advancing technology is likely to lag behind the most recent developments.

Although the general layout of this atlas is excellent, it could be improved by CT images of higher quality.

Janet E. Husband.

1979, *British Journal of Radiology*, *52*, 156

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Place of new contrast media in renal failure

THE EDITOR—SIR,

It was with great interest that I read "The effect of osmotic diuresis on urinary iodine concentration" (Webb *et al.*, 1978) in your February issue. I believe some observations from our recent experiments and calculations may be of interest and cast some additional light on the place of contrast media of reduced osmolality in advanced renal failure.

In patients with normal renal function the urinary tract increases in volume during osmotic diuresis (Dorph *et al.*, 1977) and therefore both the increase in urine flow and the iodine concentration will be of importance for the absorption of X-ray in the urinary tract. Calculations (Golman 1977) have shown that the urinary iodine concentration is the most important parameter.

In renal failure the urinary tract may be chronically fully distended by the obligatory (urea) diuresis and the contrast media may be unable to produce any further increase in the diameter of the tubulus (the depth of the X-ray absorbing layer). The urinary iodine concentration thus becomes the only parameter of importance and the significant increase in iodine concentrations obtained using metrizamide instead of the ionic media during the important first 20 min after injection in the study of Webb and colleagues (during both moderate and large mannitol diuresis) could give the increase in X-ray absorption which was just necessary to obtain a diagnostically usable examination.

Moreover, the reduced toxicity and pharmacological side-effects of metrizamide compared to the common ionic media (see Acta Radiologica Supple. 335, various authors 1973; Kolbenstvedt *et al.*, 1979) should be especially important in the presence of renal failure, as the patients may already be out of fluid balance.

In children with renal failure where the doses tend to be high per kg body weight the dehydration produced by the ionic media may produce a life-threatening condition and thus the place of contrast media of reduced osmolality must be seriously considered.

Yours, etc.,
K. GOLMAN.

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REFERENCES

DORPH, S., SOVAK, M., TALNER, L. B., and L. ROSEN, 1977. Why does kidney size change during i.v. urography? *Investigative Radiology*, *12*, 246.

GOLMAN, K., 1977. Physiological consideration on the excretion of contrast media. *Journal Belge de Radiologie*, *60*, 229.

KOLBENSTVEDT, A., ANDREW, E., CHRISTOPHERSEN, B., GOLMAN, K., KVARSTEIN, B., and LIEN, H. H., 1979. Metrizamide (Amipaque) in high-dose urography. *Acta Radiologica* (in press).

Artefacts in CT scanning

THE EDITOR—SIR,

CT-scanning is penetrating diagnostic medical practice at an amazing pace with a wide spectrum of application. Various factors of a technical nature can interfere with the diagnostic quality of the CT-scans, and among them are the introduction into the patient of radiopaque substances of high atomic number. These substances when irradiated produce hard scatter radiation which can obliterate complete sets of CT-scans, making them unreadable on account of artefacts.

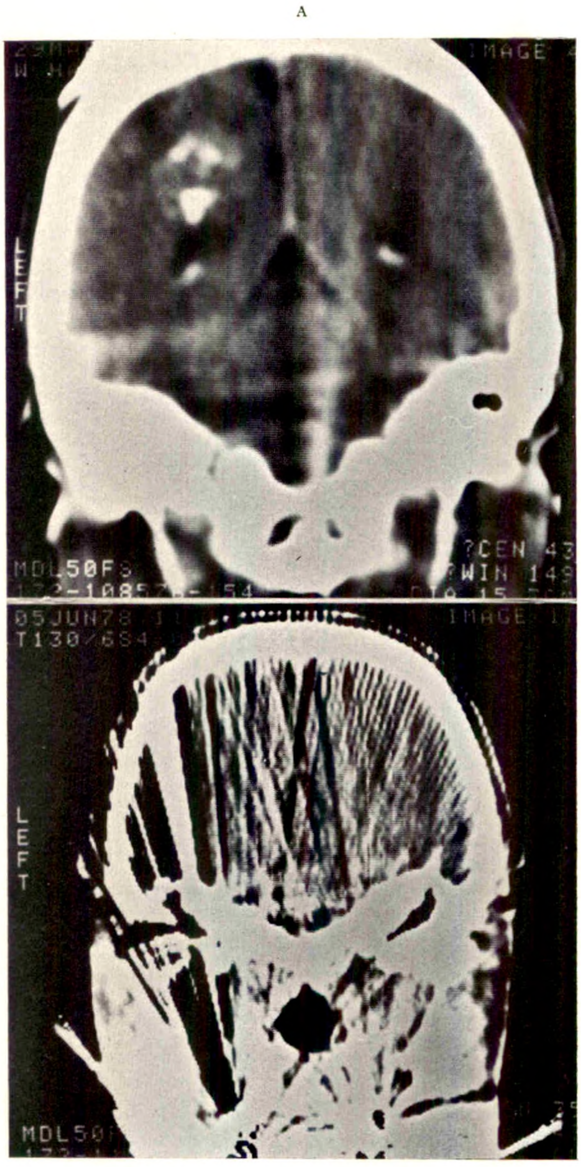

FIG. 1.

(A) A coronal section of the head of a patient with intracerebral calcification as seen before dental treatment.

(B) The disastrous effect of dental fillings on control CT-scans four weeks later

Correspondence

In this letter we address our colleagues, the dentists, to avoid as far as possible the use of dental metal alloys and to replace them by fillings and prostheses in plastic or porcelain. We invite our colleagues the anaesthetists, to replace metallic accessories for intubation by materials in plastic. We wonder if the use of neuroleptics instead of general anaesthesia, requiring no intubation, could be the best solution. We should like to ask our colleagues the neurologists and neurosurgeons to stop using oily contrast in the examination of the central nervous system, because of the residual deposits and to substitute water-soluble contrast instead. We invite them to attempt to find ways to replace metallic clips used in surgical procedures, because they are the source of most disturbing artefacts during CT-scanning.

To illustrate what we mean by artefacts produced by high atomic number substances introduced into a patient, we refer to Fig. 1A and 1B.

Yours, etc.,
J. A. Veiga-Pires,
M. Kaiser.

X-ray Department,
Academisch Ziekenhuis Utrecht
The Netherlands.

Erosion of the sphenoid bone

The Editor—Sir,

This letter has been prompted by a recent article in the Journal (May 1978) by Witcombe and Cremin describing tuberculous erosion of sphenoid bone. The purpose of this letter is to draw attention to the fact that non-specific inflammatory sinusitis may also cause extensive lytic destruction of the sphenoid bone.

Recently a 22-year-old aboriginal man was admitted to the Royal Perth Hospital with one month's history of headaches. On examination, he was apyrexial; high mental function tests, cranial nerves and rest of the central nervous system examination was normal. Skull radiographs revealed pansinusitis with destruction of the floor of the sella turcica and of the clivus. (Fig. 1).

Radiological differential diagnoses offered were chronic granulomatous infection or neoplastic (lymphomatous) destruction of the sphenoid bone. Pneumoencephalogram revealed normal cerebrospinal fluid with normal basal cisterns. Exploration of the sphenoid sinus was carried out. Bacteriological examination was negative and histology revealed non-specific inflammatory polypoidal hypertrophy of the sphenoid sinus mucosa. No evidence of tuberculosis, fungal disease or malignancy was detected.

We were fairly confident that this extensive destruction of the sphenoid bone wax due to tuberculous or fungal disease and were very surprised when this was not confirmed at operation.

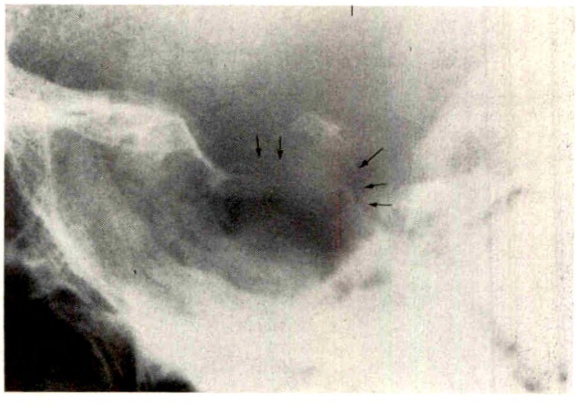

FIG. 1.

Yours etc.,
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(*Received October 1978*)

REFERENCES

Witcombe, J. B. and Cremin, B. J., 1978. Tuberculous erosion of the sphenoid bone, *British Journal of Radiology*, *51*, 347–350.

Newton, T. H., and Potts, D. G., 1971. *Radiology of the Skull and Brain*, *1*, *Book 2*, p.735 (St. Louis, C. V. Mosby).

Di Chiro, G., and Anderson, W. B., 1965. The clivus. *Clinical Radiology*, *16*, 211–223.

Carcinoma of the cervix at the Royal Marsden Hospital, London, 1962–70: survival results

The Editor—Sir,

In 1944 a joint clinic was formed by the Royal Marsden Hospital and the Chelsea Hospital for Women for the treatment of cancer patients requiring radiotherapy, and four reports on the treatment results have been published (Blaikley *et al.*, 1952, 1957, 1962, 1969). This letter presents the survival of all previously untreated patients with carcinoma of the cervix, almost 1000, seen at the Royal Marsden Hospital, London, between 1962 and 1970, some 50% of whom were also seen in the joint clinic with the Chelsea Hospital. The survival rates (Fig. 1) were calculated by an actuarial method, whereas in the earlier reports only a crude survival rate was given. However, since not more than 10% of the cases were lost to follow-up in those analyses, a valid comparison can be made between the previously published five-year survival rates and those for the 1962–70 period.

The total number in all stages is 995. Fifty were in stage 1A and 254 in stage 1B. The histology of the majority was squamous cell carcinoma. Adenocarcinomata accounted for only 8% of the entire 1962–70 series and the numbers are therefore too small for an analysis of survival rate by histology.

The overall five-year survival rates are compared with those of other series in Table I. There has been an improvement in the stage 1 results since the last RMH-Chelsea Hospital report for 1944–60, but the overall results for stages 2, 3 and 4 show no improvement, which is disappointing. The results in this current series are similar to those reported from other centres in the United Kingdom but they are significantly worse than those reported by Fletcher (1973). This is part of a pattern in which the survival of patients with carcinoma of the cervix in the United Kingdom is generally lower than the survival reported from North America, although the reasons for the existence of such a pattern are not certain.

We wish to thank Dr. M. Lederman and Dr. V. M. Dalley for their encouragement with this study and for permission to use their data. We are also grateful to Mr. R. B. Rickford

TABLE I
Five-year carcinoma cervix survival rates

Stage	Hospital series					
	*Royal Marsden 1962–70	†Royal Marsden and Chelsea 1944–60	†Manchester 1961–65	*Houston 1954–67	†124 institutions in 26 countries 1956–60	*Royal Marsden Chelsea Hammersmith U.C.H. Middlesex 1944–72
1	74%	64%	73%	92%	76%	71%
2	46%‡	45%	52%	76%§	54%	48%
3	16%	19%	25%	41%¶	32%	21%
4	6%	4%		14%	8%	Not stated
Total cases	995	1007	1991	1705	32774	2829
Reference		Blailkey *et al.* (1969)	Easson (1973)	Fletcher (1973)	Ackerman and del Regato (1970)	Mould (1973)

*Actuarial survival rate calculation.
†Crude survival rate calculation.
‡Five-year survival rates for stage 2A were 51% and for stage 2B were 43%.
§Mean five-year survival rates calculated from stage 2A (84%) and stage 2B (67%).
¶Mean five-year survival rates calculated from stage 3A (45%) and stage 3B (36%).

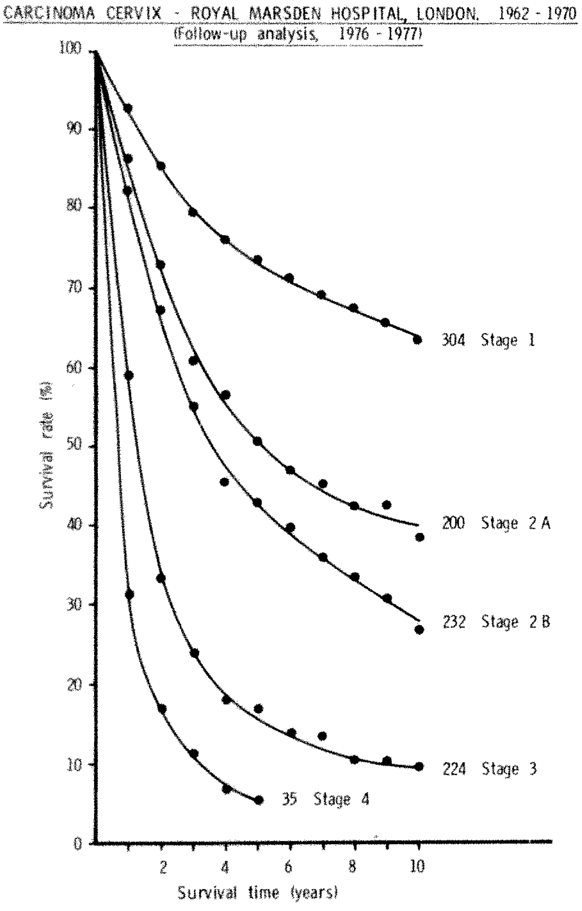

Fig. 1.

and all referring gynaecologists. We would also like to thank Mrs. V. S. Chapman for secretarial assistance.

Yours, etc.,
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Jean F. Staffurth.

Radiotherapy Department,
Royal Marsden Hospital,
London, S.W.3.

REFERENCES

Ackerman, L. V., and del Regato, J. A., 1970. In *Cancer*, chap. 14 (C. V. Mosby, St. Louis, using data from Kottmeier, H.-L., Annual report on the results of treatment in carcinoma of the uterus and vagina, vol. 14, Stockholm, 1967, P. A. Norstedt and Soner).

Blaikley, J. B., Lederman, M., and Lewis, T. L. T., 1952. Carcinoma of the cervix at Chelsea Hospital for Women, 1933–1951. *Lancet*, *2*, 950–951.

Blaikley, J. B., Lederman, M., and Simmons, C. A., 1957. Carcinoma of the cervix at Chelsea Hospital for Women, 1933–1956. *Lancet*, *2*, 1329–1333.

Blaikley, J. B., Lederman, M., and O'Connor, K. J., 1962. Carcinoma of the cervix at Chelsea Hospital for Women, 1933–1960. *Lancet*, *2*, 978–984.

Blaikley, J. B., Lederman, M., and Pollard, W., 1969. Carcinoma of the cervix at Chelsea Hospital for Women, 1933–1965. *Journal of Obstetrics and Gynaecology*, *8*, 729–784.

Easson, E. C., 1973. In *Cancer of the Uterine Cervix*, chap. 8 (Saunders, London).

Fletcher, G. H., 1973. In *Textbook of Radiotherapy*, chap. 11 (Lea and Febiger, Philadelphia).

Mould, R. F., 1973. Statistical models for studying long term survival results following treatment for carcinoma of the cervix. Ph.D. thesis, London University.

1979, *British Journal of Radiology*, 52, 159–160 FEBRUARY 1979

Correspondence

Relative efficacy of high-pressure oxygen and misonidazole to reduce TCD50 of a mouse mammary carcinoma

THE EDITOR—SIR,

Respiration of pure oxygen at 200 kPa (30 psi) before and then during each treatment session of conventional fractionated radiation therapy has recently been found to improve survival rates for patients with squamous carcinomas of the head and neck (Henk and Smith, 1977), uterine cervix (Watson *et al.*, 1978) and bronchus (Cade *et al.*, 1978). For the head and neck and the uterine cervix group (Stage III), local control frequencies were increased by some 20 percentage points: indeed an impressive improvement. These data provide strong support for the concept that some of the failures of conventional radiation therapy are due to the presence of hypoxic and hence radiation-resistant tumour cells (Gray *et al.*, 1953). Thus, these data constitute a clear stimulus for further efforts to develop effective means to overcome the impact of hypoxic cells on radiation therapy. Technical complexity and clinical limitations in the use of hyperbaric oxygen, together with the very long time which was required in obtaining positive results from the clinical trials mentioned above have, we think, been important contributions to the decrease in level of interest in the use of hyperbaric oxygen. The major current laboratory and clinical investigations of this general problem are directed towards assessment of the clinical efficacy of high LET radiation and of compounds which selectively radiosensitize hypoxic cells. However, results from prospective clinical trials of high LET radiations (Catterall *et al.*, 1977) hypoxic sensitizers (Urtasun *et al.*, 1976) are, by comparison with those available for high pressure oxygen, very limited. There have been no comparisons of the efficacy of these various approaches to the problem of hypoxic cells using laboratory animal models.

Results from TCD50 assays of the C3H mouse mammary carcinoma, MDAH/MCaIV for radiation given under conditions of hyperbaric oxygen respiration or of misonidazole treatment are of interest in this context. Data from single dose and fractionated irradiation (ten equal doses, one day between fractions) of this tumour but performed at different laboratories and at different times are presented in Table I. Enhancement ratios are computed as TCD50 air/TCD50 test for studies with O_2 at 200 kPa or misonidazole. The results from these two sets of experiments demonstrate that hyperbaric oxygen was impressively more effective in reducing the TCD50 for fractionated radiation than was misonidazole. However, misonidazole at both 0.3 mg/g body weight and 1.0 mg/g were more effective for single dose irradiation than was hyperbaric oxygen. Our confidence in the results of this inter-laboratory comparison is strengthened by the fact that the enhancement ratio for misonidazole and single dose irradiation for MDAH/MCaIV studied under the same conditions was 2.3 (Stone and Withers 1975), *i.e.*, identical to the value found at Stanford.

The enhancement ratio of misonidazole shown in this table for ten fractions of radiation is consistent with the enhancement ratio of 1.2 to 1.5 for two other tumour systems irradiated with five fractions over four days (Fowler *et al.*, 1976; Sheldon and Hill, 1977). In assays of fractionated irradiation and hyperbaric oxygen with this tumour, enhancement ratios for radiation given in five to ten fractions with inter-treatment intervals of less than one day up to five days have been in the range 1.6 to 1.8 (Suit *et al.*, 1977).

These various data suggest that the results of combining misonidazole at maximum tolerated doses with fractionated irradiation will not necessarily be superior to those obtained by combining high pressure oxygen with fractionated irradiation. Because of the very large body of clinical data on the efficacy of hyperbaric oxygen there is now a serious need for studies of the comparative efficacy of hyperbaric oxygen, hypoxic cell sensitizers and high LET radiation based on data generated in one laboratory using several different animal tumour systems.

Yours, etc.,

H. D. SUIT,

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J. M. BROWN.

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Stanford, CA 94305.

TABLE I

TCD50 VALUES FOR 8 MM MDAH/MCA IV FOR SINGLE OR FRACTIONATED IRRADIATION ALONE OR COMBINED WITH O_2 AT 200 KPA (30 PSI) OR MISONIDAZOLE

Investigator	Treatment: Radiation	Treatment: Modifier	TCD50 (rad) (95% Conf. limits)	Enhancement Ratio (95% Conf. intervals)
Suit *et al.*, (1977)	^{137}Cs	Respired gas		
	$\nu = 1$	AIR	6550 (6320 ... 6790)	1.12 (1.04 ... 1.21)
		O_2 30 psi	5830 (5420 ... 6270)	
	$\nu = 10$*	AIR	10450 (9490 ... 11500)	1.78 (1.56 ... 2.01)
		O_2 30 psi	5850 (5370 ... 6380)	
	$\nu = 10$	AIR	10570 (9680 ... 11540)	1.72 (1.50 ... 1.98)
	(repeat)	O_2 30 psi	6140 (5490 ... 6870)	
Brown (1978)	250 kV	Misonidazole†		
unpublished	$\nu = 1$	0.0	7125 (6600 ... 7700)	
		0.3 mg/g	< 4000	> 1.8
		1.0 mg/g	3100 (2960 ... 3250)	2.30 (2.10 ... 2.51)
	$\nu = 10$	0.0	9700 (8660 ... 10860)	1.39 (1.23 ... 1.56)
		0.3 mg/g	7000 (6730 ... 7200)	

*10 equal doses, 1 day between treatments.
†injection of drug i.p. 30 min prior to start of radiation exposures.
ν is the number of fractions.

1979, *British Journal of Radiology*, 52, 160–161

REFERENCES

Cade, I. S., McEwen, J. V., Dische, S., Saunders, M. I., Watson, E. R., Halnan, K. E., Wiernik, G., Perrins, D. J. D., and Sutherland, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial of carcinoma of the bladder. *British Journal of Radiology*, *51*, 876–878.

Catterall, M., Bewley, D. K., Sutherland, I., 1977. Second report on results of a randomized clinical trial of fast neutrons compared with χ or gamma rays in treatment of advanced tumours of head and neck. *British Medical Journal*, *1*, 1642.

Fowler, J. F., Sheldon, P. W., Denekamp, J., and Field, S. D., 1976. Optimum fractionation of the C3H mouse mammary carcinoma using X-rays, the hypoxic cell radiosensitizer RO–07–0582, or fast neutrons. *International Journal of Radiation Oncology, Biology, Physics*, *1*, 579–592.

Gray, L. H., Conger, A. D., Ebert, M., Hornsey, S., and Scott, O. C. A., 1953. The concentration of oxygen dissolved in tissues at the time of irradiation as a factor in radiotherapy. *British Journal of Radiology*, *26*, 638–648.

Henk, J. M., and Smith, C. W., 1977. Radiotherapy and hyperbaric oxygen in head and neck cancer. *The Lancet*, *2*, 104–105.

Sheldon, P. W., and Hill, S. A., 1977. Further investigations of the hypoxic cell radiosensitizer, RO–07–0582, on local control of a mouse tumour. *British Journal of Cancer*, *36*, 198–205.

Stone, H. B., and Withers, H. R., 1975. Enhancement of the radioresponse of a murine tumour by a nitroimidazole. *British Journal of Radiology*, *48*, 411–412.

Suit, H. D., Howes, A. E., and Hunter, N., 1977. Dependence of response of a C3H mammary carcinoma to fractionated irradiation on fractionation number and intertreatment interval. *Radiation Research*, *72*, 440–454.

Urtasun, R., Band, P., Chapman, J. D., Feldstein, M. L., Mielke, B., and Fryer, C., 1976. Radiation and high-dose metronidazole in supratentorial glioblastomas. *New England Journal of Medicine*, *294*, 1364–1367.

Watson, E. R., Halnan, K. E., Dische, S., Saunders, M. I., Cade, I. S., McEwan, J. B., Wiernik, F., Perrins, D. J. D., and Sutherland, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial in carcinoma of the cervix. *British Journal of Radiology*, *51*, 879–887.

Two regimes with the same TDF but differing morbidity used in the treatment of stage III carcinoma of the cervix

The Editor—Sir,

In the above-named paper, Singh (1978) reports his clinical experience in treating cervix patients with daily or weekly fractionation schedules using ^{60}Co radiation as part of more complex treatment regimes. I disagree with the conclusions which he draws from an analysis of the late reactions or complications found in these patients.

Patients presenting with stage IIIB carcinoma of the cervix were treated with complex regimes comprising a parallel-opposed fractionated schedule preceding a radium insertion, followed in turn by a further parallel-opposed fractionated schedule, as a general protocol. The patients were divided into two groups: Group I having fractionated schedules given daily and Group II weekly. As similar radium treatments were given to both groups, it is reasonable to attribute the differences in morbidity found to the different fractionated schedules used and to ignore the radium treatment in this discussion. In Group I, patients with separations greater than 18 cm were given 3000 rad (all quoted doses are mid-plane) and thinner patients 4000 rad in 20 daily fractions, from the first parallel-opposed schedule. All patients in this group were given 1000 rad in five daily fractions after the radium insertion. Presumably the dose to mid-plane for thicker patients was reduced to minimize the doses to subcutaneous and underlying tissues. In Group II, all patients regardless of thickness were given five fractions of 580 rad in 28 days before radium insertion, and one fraction of 670 rad after insertion, although this latter dose was on occasion reduced to 580 rad. These treatment schedules given to Group II were assessed as being equivalent to the corresponding schedules of 4000 rad in 20 daily fractions and 1000 rad in 5 daily fractions of Group I on the basis of the TDF tables of Orton and Ellis (1973).

I take issue with the conclusions reached by Singh (1978) on two counts. The CRE-system (Kirk *et al.*, 1971) suggests that the equivalent single fraction given after insertion in Group II should have been 550 rad rather than 670 rad to have the same biological effect as 100 rad given in five daily fractions (the CRE can be applied to one fraction if part of an extended regime). However, of greater significance is the fact that apparently all patients in Group II were given a treatment schedule before insertion assessed as being equivalent to 4000 rad given in 20 fractions in four weeks (TDF of 66), and no reduction in dose was made for patients with separations greater than 18 cm as in Group I. Therefore, such patients would receive higher incident doses and consequently higher doses to subcutaneous and underlying tissues, so that it is not surprising to find a greater incidence of late reactions and complications in Group II. The conclusions reached by Singh (1978) from an analysis of the results of his clinical trial are based on the false premise that he has compared the radiation reactions of two groups of patients given equivalent regimes; although "equivalence" and "validity" of empirical descriptions of biological effect are also on test. In fact, by not modifying the dose with thickness of patient in Group II but doing so in Group I, the two groups of patients have been treated according to completely different policies, so that the objectives of the clinical trial have not been achieved.

However, while criticizing the conclusions reached on the basis of existing data, I fully appreciate the practical merits in the prevailing local conditions of changing from daily to weekly fractionation schedules, and it would be a pity at this stage to abandon the possibility of using weekly fractionation. It is evident from Singh (1978) that late reactions and complications are the limiting factors. In a detailed study, involving clinical trials, of fractionation and dose-rate in radiotherapy (Turesson, 1978), Turesson and Notter thoroughly investigated the matter of early and late reactions on the basis of skin response. As a result, they have presented a modified form of the CRE formulation for assessing the late reactions of fractionated treatment schedules. Assuming the relevance of that equation to the present situation, the following treatment regimes for Group II are proposed as equivalent to those used in Group I for late effects:

(a) for separations greater than 18 cm:
  five fractions of 410 rad given in 28 days before the radium insertion, followed by a single fraction of 520 rad,
(b) for separations of 18 cm or less:
  five fractions of 540 rad given in 28 days before the radium insertion, followed by a single fraction of 520 rad.

While empirical descriptions of biological effect such as the NSD, TDF and CRE may not necessarily be applicable to the rectosigmoid, validity can not be disproved on the basis of the evidence presented by Singh (1978).

Yours, etc.,
J. Kirk.

West of Scotland Health Boards,
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Scotland.

Correspondence

REFERENCES

KIRK, J., GRAY, W. M. and WATSON, E. R., 1971. Cumulative radiation effect. Part I: fractionated treatment regimes. *Clinical Radiology*, *22*, 145–155.

ORTON, C. G. and ELLIS, F., 1973. A simplification in the use of NSD concept in practical radiotherapy. *British Journal of Radiology*, *46*, 529–537.

SINGH, K., 1978. Two regimes with the same TDF but differing morbidity used in the treatment of Stage III carcinoma of the cervix. *British Journal of Radiology*, *51*, 357–362.

TURESSON, INGELA, 1978. Fractionation and dose rate in radiotherapy. An experimental and clinical study of Cumulative Radiation Effect. (Thesis Ch. III, pp. 31–37, Unixersity of Göteborg, Sweden.)

(*In reply*)

Two regimes with the same TDF but differing morbidity used in the treatment of stage III carcinoma of the cervix

THE EDITOR—SIR,

I am grateful to Dr. Kirk for his comments and suggestions. His letter has provided me with an opportunity to remove any ambiguity in my paper.

In Group I, three patients with a separation above 18 cm were given a midplane dose of 3000 rad prior to intracavitary insertion. These patients were, however, given the remaining 1000 rad to the whole pelvis after the intracavitary insertion. I had stated in my paper: "A total dose of 8000 rad was given to point A and 6000 rad to the pelvic wall. The central high dose area was shielded after the whole pelvis had received 4000 rad by cobalt." Thus all patients in Group I received 4000 rad to the whole pelvis by cobalt teletherapy. We had planned to do the same in Group II; those with a separation greater than 18 cm to get only four (instead of five) weekly fractions prior to intracavitary irradiation and two (instead of one) weekly fractions after the intracavitary irradiation. It was by chance that no patient in this group had a separation exceeding 18 cm. To make it absolutely clear: the mid-pelvic dose was the same in each patient irrespective of the separation. I did not reject patients with a greater separation from Group I because I did not want to vitiate the trial by any selection. Consecutive patients were therefore included in both the groups.

I must admit that I was not clear as to the equivalent single dose after the insertion. This dose was meant for irradiation of the parametria with central shielding. As pointed out by Dr. Kirk this dose was high but I doubt if this slightly higher dose to the parametria contributed to the severity of the rectal reactions.

I highly appreciate the suggestion of Dr. Kirk of not abandoning the weekly regime but to repeat the trial with the dose schedules calculated by him on the basis of Turesson's work. I do not think there is any need to reduce the dose for patients with a separation greater than 18 cm.

Yours, etc.,
K. SINGH.

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Education and Research,
Chandigarh, India.

Computer assistance: an essential for adrenal imaging

THE EDITOR—SIR,

We read with interest the recent report (Thomson *et al.*, 1978) in your journal of the successful visualization of abnormal adrenal uptake without the use of computerized background subtraction. Our recent experience with two different adrenal scanning agents and a variety of imaging devices leads us to agree that computer assistance is not routinely required for diagnostic purposes, although it is essential for quantifying adrenal uptake (Koral and Sarkar, 1977).

Our initial experience of adrenal imaging with ^{131}I–19–iodocholesterol in 46 patients was recently reported (Wahner *et al.*, 1977) and since that time we have studied a further 65 patients with ^{131}I–6β–iodomethyl–19–norcholest–5–(10)–en–ol (NP 59). This series of 111 patients includes 57 with primary aldosteronism and 30 who fulfil the clinical and biochemical criteria of Cushing's syndrome. During the earlier studies we employed for imaging purposes either a rectilinear scanner or a wide-field gamma camera. More recently we have routinely used a Pho/Con (Searle Radiographics, Inc.) Emission Tomographic Scanner.

In our hands the images obtained by the tomographic scanner represent a significant advance over those obtained by either the rectilinear scanner or a conventional gamma camera. Although routinely we obtain computerized images with background subtraction and smoothing we have not found this facility essential for the provision of diagnostic information.

Although we feel that using the computer "as a means of subtracting unwanted uptake" (Thomson *et al.*, 1978) is not a necessity for routine adrenal imaging, we do, however, successfully employ the computer in a rather different context. Using a recently described subtraction technique (Thorson *et al.*, 1978) we obtain an accurately defined renal or liver image with ^{99}Tc^{m} DTPA or ^{99}Tc^{m} sulphur colloid respectively and after renal or liver localization we employ the computer to further define the location of the adrenal image. An example of this technique is shown in Fig. 1 (p. 162) which demonstrates a right sided aldosteronoma in a patient with Conn's syndrome.

Yours etc.,
I. D. HAY,
M. L. BROWN,
H. W. WAHNER.

Division of Endocrinology and
Department of Diagnostic Nuclear Medicine,
Mayo Clinic, Rochester,
Minnesota 55901 USA

(*Received September, 1978*)

REFERENCES

KORAL, K. F. and SARKAR, S. D., 1977. An operator-independent method for background subtraction in adrenal-uptake measurements. *Journal of Nuclear Medicine*, *18*, 925–928.

THOMSON, D. M., DOVEY, P. P., and DAVIS, J. B., 1978. Visualization of abnormal adrenal uptake of 19–iodocholesterol in Conn's syndrome. *British Journal of Radiology*, 51, 545–546.

THORSON, L. M., BECKER, G. P., and WAHNER, H. W., 1978. Subtraction technique in the diagnosis of abdominal abscesses. *Journal of Nuclear Medicine Technology*, 6, 11–16.

WAHNER, H. W., NORTHCUTT, R. C., and SALASSA, R. M., 1977. Adrenal scanning: usefulness in adrenal hyperfunction. *Clinical Nuclear Medicine*, 2, 253–264.

1979, *British Journal of Radiology*, *52*, 162

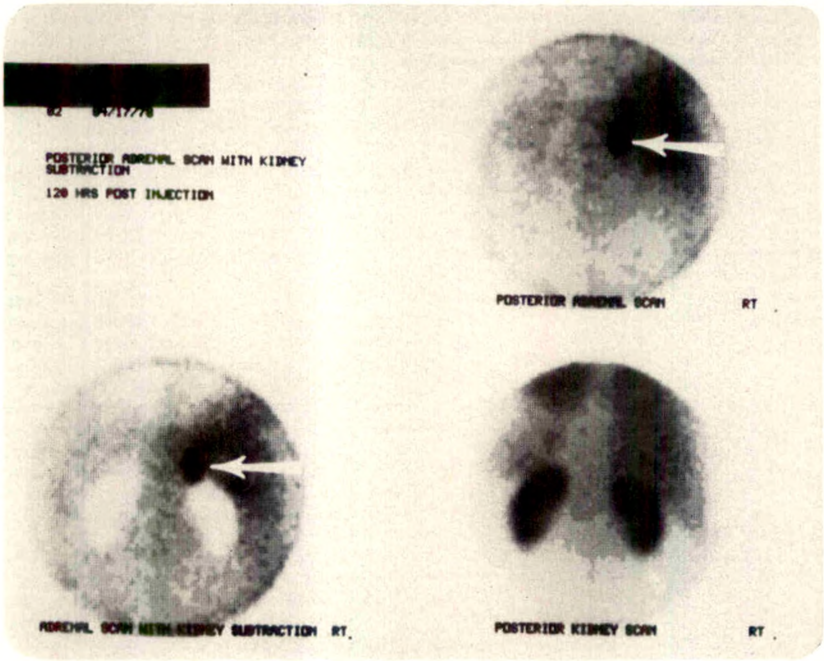
[redacted]
POSTERIOR ADRENAL SCAN WITH KIDNEY SUBTRACTION
120 HRS POST INJECTION
POSTERIOR ADRENAL SCAN RT
ADRENAL SCAN WITH KIDNEY SUBTRACTION RT
POSTERIOR KIDNEY SCAN RT

FIG. 1.

Tomographic scans of patient with Conn's syndrome 120 hours after injection. Posterior view (top right), kidney scan (bottom right), adrenal with kidney subtracted (bottom left).

The centigray as the SI unit of dose

THE EDITOR—SIR,

Dr. Halnan asks (Halnan, 1978) for support for the use of the centigray (cGy) as the practical SI unit of dose for clinical radiotherapy. We wish to offer our support, and endorse his reasons. We have in mind particularly those circumstances where dose is prescribed as, for example, 60 rad (0.6 Gy) daily, or in the case of total body treatments say 10 rad (0.10 Gy) and where serious error could arise in association with the use of the gray. In addition, although many treatment doses may be in kilorad, dose rates are generally of the order of 1 Gy per minute and are often below that figure. (Were we under any threat of being forced to express dose rates in s^{-1} rather than min^{-1} there would be a problem of even greater concern.)

We see no reason why a department should not, if it wishes, use the centigray strictly for internal, everyday, routine purposes and use the gray in formal papers, annual reports, or any other documents going out of the department. Indeed, if such a department continued on this basis to call the centigray unit the "rad" we do not see that anyone outside that department would have cause to complain. Units should be for the convenience of the user.

It must be recognized that the millirad cannot very well be perpetuated as the milli-centigray. However, the millirad has never had such strong claims as a practical unit in protection as has the rad in radiotherapy. For practical use the mSv and μSv are probably on balance neither better nor worse than the rad and mrad, though we have seen little published discussion of that point.

A recent report of BCRU, widely circulated for comment, expressed at least tolerance and even slight encouragement for the centigray in radiotherapy. A revised version of this report confirms that tolerance.

Yours, etc.,
W. DUNCAN,*
J. LAW.†

Departments of Radiation Oncology* and Medical Physics and Medical Engineering,†
Western General Hospital,
Edinburgh EH4 2XU.

(*Received June, 1978*)

REFERENCE

HALNAN, K. E., 1978. The centigray as the SI unit of dose. *British Journal of Radiology*, *51*, 395.

SI units in radiotherapy

THE EDITOR—SIR,

We note with concern recent correspondence advocating the use of the centigray as a unit of dose (Halnan 1978, Martin-Smith 1978). Considering the reasoning and history behind the introduction of the SI system, it would be a retrograde step to introduce a unit such as the centigray.

As the Australian Metric Conversion Board recommended that Australians adopt the SI units in radiotherapy by January 1978, the Cancer Institute, Melbourne changed to these units (rad to gray and centimetre to millimetre) on October 3, 1977.

It was thought that with proper prior instruction experienced staff would have no difficulty in adapting to the new units. The date was chosen so that final year students would have time to adapt to the new units before becoming fully qualified at the end of the Australian academic year in December.

It was decided to use the gray to express both total doses and fractions rather than complicating matters by using the milligray. Settings and displays of monitor units on therapy machines were readily converted so that they bore the same relationship to the gray as they formerly did to the rad. Outputs of orthovoltage and superficial machines were given in terms of seconds per gray, as this retained reasonable sized numbers without going to submultiples and preserved the intentions of the SI system.

It need hardly be added that the same number of significant figures are used in the ordering of doses, setting of monitor units and time, etc., and that there is no reduction in accuracy.

During the period October 3, 1978 to June 30, 1978, 4588 new courses of external beam radiotherapy were planned and treated and a total of 93 587 fields were delivered. All reported errors during this time were reviewed and none were directly or indirectly attributable to the change of units.

In conclusion, our experience shows that even in a very large radiotherapy centre a change to SI units need not be a traumatic one; there was no sign of an increased error rate and there has been no decrease in accuracy.

Yours etc.,
T. F. SANDEMAN,
R. M. MILLAR,
J. D. DRUMMOND.

Cancer Institute,
481 Little Lonsdale Street,
Melbourne, Victoria, 3000,
Australia.
(*Received October, 1978*)

REFERENCES

HALNAN, K. E., 1978. The centigray as the SI unit of dose. *British Journal of Radiology*, *51*, 395.

MARTIN-SMITH, P., 1978. The centigray as the SI unit of dose. *HPA Bulletin*, August, 71.

Metric Conversion Board (Australia), May 1977. Units for the Measurement of Radioactivity and of Ionising Radiation.

X-ray visibility of the dark adapted eye

THE EDITOR—SIR,

With reference to Dr. Cochrane Shanks' recent letter (1978), the fact that X-rays are visible to the dark adapted eye is not generally known, but in fact it was noted by Röntgen and several of the early workers.

Similar observations were made with radium. It has also been suggested, though not recently, that these properties could be used to help the partially blind to see.

I published with Professor Arnold Sorsby (Sorsby and O'Connor, 1945; Deller *et al.*, 1947) a method of measuring the diameters of the living eye, making use of this property. It is interesting that this should have been again noticed by Dr. Shanks in the context of the modern CAT scanner.

Yours, etc.,
A. D. O'CONNOR.

Department of Radiotherapy & Oncology,
King's College Hospital,
Denmark Hill, London SE5 9RS.
(*Received October, 1978*)

REFERENCES

COCHRANE SHANKS, S., 1978. CAT stimulation of retina. *British Journal of Radiology*, *51*, 837.

SORSBY, A., and O'CONNOR, A. D., 1945. Measurement of the diameters of the living eye by means of X-rays. *Nature*, *156*, 779.

DELLER, J. F. P., O'CONNOR, A. D., and SORSBY, A., 1947. X-ray measurement of the diameters of the living eye. *Proceedings of the Royal Society*, *134*.

Sensitivity of the eye to X rays

THE EDITOR—SIR,

Many readers will have been interested in Dr. Cochrane Shanks' brief report on the sensation of light he experienced whilst undergoing an EMI scan (Cochrane Shanks, 1978). Few of us could confirm this observation from our own experience and this is testimony to the progress that has been made in radiation safety.

Some years ago, browsing in Manchester University Library, I happened upon a book which, so far as I recall, was Clark(e), Applied X-rays, 1936. In it I found the comment, again to the best of my memory, "Every radiation worker will be familiar with the sensation of light which is experienced when a beam of X-rays impinges on the eyes".

Yours, etc.,
E. W. EMERY.

Department of Medical Physics,
Royal Postgraduate Medical School,
Hammersmith Hospital,
Du Cane Road, London W12 OHS.
(*Received October, 1978*)

REFERENCE

COCHRANE-SHANKS, S., 1978. CAT stimulation of retina. *British Journal of Radiology*, *51*, 837.

Alterations in the manuscript of Röntgen's publication "Ueber eine neue Art von Strahlen" (1895)

THE EDITOR—SIR,

We are extremely interested in the letter to the editor by Dr. E. Fischman (Fischman, 1978).

Dr. Fischman contends that Dr. Freund in his article "Lenard's share in the discovery of X-rays", in the 1946 issue of your journal, was probably incorrect in assuming that Röntgen experimented with a Lenard tube when on November 8, 1895 he discovered "A New Kind of Ray." Dr. Fischman clearly points out that the analysis of the first page of the manuscript does not support the contention that it was a Lenard tube.

Dr. Kraft's research and our translation of Zehnder's correspondence with Röntgen indicated that, although Röntgen discovered the X ray in 1895, the question of whether a Lenard tube was utilized in the crucial experiments was raised first in 1901. Until that time, Röntgen had remained uncontested in his discovery. However, when he was awarded the Nobel Prize in 1901, Lenard felt chided as he considered himself the true discoverer.

Röntgen used to keep his tubes attached to mercury pumps for several days at a time in order to obtain a near perfect vacuum. Lenard's aluminium-window tube apparently proved less suitable for this purpose. If it were otherwise, Röntgen would have undoubtedly given Lenard his due credit.

Zehnder, in his comments to Röntgen's letters to him, stated that on his visit to Würzburg in 1896, soon after the discovery, Röntgen told him that he had made the discovery with a Hittorf tube. In his letter to Zehnder, dated April 4, 1905, Röntgen wrote: "I can well understand that some physicists have not participated (nominal contribution for a memorial tablet on his 60th birthday), not necessarily due to an unfriendly attitude. Well, dear heaven, the envious are never lacking when something occurs as with me. That is always the case."

On May 15, 1921, Röntgen wrote to Zehnder: "I want to thank you for having always emphatically defended me as to the priority claim regarding the discovery of the X-ray. The false rumours, I think, started in Heidelberg with Quincke (Lenard's superior) on whose toes I have stepped a few times. Lenard, a former friend confirmed these rumours after I had moved to Munich and received the Nobel Prize."

It was earlier believed that the cathode ray caused fluorescence which occurred at a distance from the tube very close to the tube in contrast to the later discovery of an ionizing effect. With a most careful preparation for the crucial experiment, Röntgen succeeded in obtaining fluorescence for much greater distances than previously. This significant breakthrough led to the discovery of a "new kind of ray," differing from the cathode ray. Actually, this discovery was never challenged except for the breakthrough.

On the other hand, Lenard, for almost five decades, persisted that the X-ray was his own brainchild which Röntgen, acting as an obstetrician, merely extracted with forceps (interviews with O. Glasser and L. Etter after World War II) (Etter, 1946).

We, therefore agree with Dr. Fischman and disagree with Dr. Freund in believing that Röntgen's great contribution was unrelated to and not dependant upon the use of the Lenard tube.

Yours, etc.,

N. Finby,
E. Kraft.

St. Luke's Hospital Center,
Amsterdam Avenue,
114th Street,
N.Y.C. 10025.

(*Received August, 1978*)

REFERENCES

Etter, L. E., 1946. Some historical data relating to the discovery of Roentgen rays. *American Journal of Roentgenology*, *56*, 220–231.

Freund, F., 1946. Lenard's share in the discovery of X-rays. *British Journal of Radiology*, *19*, 131–132.

Fischman, E., 1978. Alterations in the manuscript of Röntgen's publication "Ueber eine neue Art von Strahlen" (1895). *British Journal of Radiology*, *51*, 475–476.

The plight of radiologists in Russia

The Editor—Sir,

Dr. Maria Slepak is alive, not very well and living at the moment in Moscow. Colleagues may know that she is a radiologist who has been convicted of "malicious hooliganism" because she and her husband had displayed a poster on the balcony of their flat demanding their long-refused right to emigrate and rejoin their family. This means that at any time, even near the end of her sentence, she can be sent to a labour camp for three years. She had four days notice of her trial, shortly after discharge from hospital where she had treatment for exacerbation of a duodenal ulcer.

You may also have read that her husband Vladimir, an electronics engineer, was exiled to Siberia to menial work for five years on June 21, 1978 on a similar charge. She will probably be permitted to join him. They are "refuseniks" of long standing, eight years, and during that time have suffered physical harassment and intimidation. On one occasion Dr. Slepak was beaten by the K.G.B. in front of her family and her son, then aged eleven, was arrested on his way home from school and threatened.

This journal is inappropriate for political matters, so it is important to differentiate between "refuseniks"—who have been refused permission contrary to the Helsinki agreement, to leave the USSR to rejoin their families—and "dissidents", such as Nobel-Prizewinner Sakharov and Dr. Orlov, whatever we may feel about the treatment meted out to these latter.

It is possible that the relatively light sentence demanded by the public prosecutor came as a result of world interest and pressure. Therefore, a group of radiological colleagues is being formed to support Dr. Slepak both morally and practically. This will require a large number of doctors each to make a very small effort.

Regrettably, it will probably be necessary also to help Dr. Alla Drugova, another radiologist, whose husband, Iosef Begun was again exiled to Siberia on June 29, 1978. His offence was to return to her in Moscow after finishing his exile,without having received permission to live in that particular city.

We should welcome a response from you by telephone or letter to Dr. Jeffrey J. Lesser, 82 Harley Street, London W.1—01-636 7171—or to Mrs. Joan Dale, 2 Frognal Rise, London N.W.3.—01-794 3324—as soon as possible.

Yours, etc.,

G. Ansell, George du Boulay,
G. de Lacey, E. Rhys Davies,
R. Dick, R. Eban, P. Gishen,
M. Goldman, R. Grainger,
B. Green, M. Grossman,
H. Highman, A. H. Isaacson,
C. D. Krasner, L. Kreel,
G. Lamb, G. Lawton,
L. Lessof, A. Lynn,
G. C. Markham, B. E. Nathan,
L. Pell, J. Rabinowitch,
P. Renton, M. I. Robinson,
T. Sherwood, M. M. Saxton,
E. Sheville, H. Shawdon,
G. F. Shepherd, S. M. Smith,
J. D. Spencer, M. Spiro,
F. Starer, G. M. Steiner,
R. F. Steiner, D. H. Trapnell,
G. H. Weinbrenn, R. A. Wilkins,
G. Whiteside.

2 Frognal Rise,
London, N.W.3.

1979, *British Journal of Radiology*, *52*, 165–166 FEBRUARY 1979

Proceedings of the British Institute of Radiology

High dose-rate afterloading gynaecological irradiation as an adjuvant to gynaecological surgery: an assessment of the cathetron

Abstracts of papers presented at a British Institute of Radiology meeting held on May 18, 1978, at the Institute House, 32 Welbeck Street, London W1

The place of the cathetron in the management of endometrial carcinoma, by C. A. Joslin.
Treatment techniques of carcinoma of cervix and endometrium at the Middlesex Hospital—early results, by Miss Margaret Snelling (*no abstract received*).
Fractionation and dose-rate relationships: formulae, experiments and clinical experience, by W. E. Liversage.
Pre-operative irradiation of uterine cancer using the cathetron, by D. O'Connell, N. Howard and M. G. R. Hull.

THE PLACE OF THE CATHETRON IN THE MANAGEMENT OF ENDOMETRIAL CARCINOMA

By C. A. Joslin

University Department of Radiotherapy
Cookridge Hospital, Leeds

Endometrial cancer is usually stage I disease suitable for surgery. Opinions differ on management but pre-operative intrauterine or post-operative intravaginal radiotherapy is invariably given. Cases considered unfit for surgery may be treated by radical radiotherapy alone. Either of these combinations may have supplementary external beam radiotherapy.

As the cathetron utilizes a single line source supplemented with vaginal ovoids in pre-operative use, it can be argued it will only produce bulk reduction and reduce viable tumour spillage. In use, one to three treatments are given in up to 14 days. Sufficient cases have yet to be reported to provide a fair assessment of results.

The cathetron is an ideally suited machine to carry out afterloading of an intravaginal obturator following surgery (Joslin and Smith, 1971). When used alone, five fractions, each of 700 rad, prescribed at 0.5 cm from the surface of the obturator, on a daily basis, is sufficient to reduce vaginal vault deposits to one in 88 cases. The advantages include outpatient treatment taking a few minutes and the ease of combining with external beam therapy.

A reduction in cathetron dose to 2000 rad in four fractions with 3500 rad teletherapy in 16 fractions over 28 days is used for combined treatment. Combined treatment is particularly indicated where lymph node involvement is suspected (Joslin *et al.*, 1977).

Overall cure rates in 256 cases have improved by 10% at five years compared with 280 cases having restricted radiotherapy before the cathetron ($p < 0.01$). The morbidity is no worse than that for low activity sources.

For radical treatment alone the cathetron has little to offer a medically unfit patient because of the number of treatments involved. It also suffers the disadvantages of a single line source although attempts are being made to overcome this.

REFERENCES

JOSLIN, C. A. and SMITH, C. W., 1971 Post-operative radiotherapy in the management of uterine corpus carcinoma. *Clinical Radiology*, *22*, 118–124.

JOSLIN, C. A., VASIHAMPAYAN, G. V. and MALLIK, A., 1977. The treatment of early cancer of the corpus uteri. *British Journal of Radiology*, *50*, 38.

Reprints of these abstracts may be obtained free on application to the Managing Editor, BRITISH JOURNAL OF RADIOLOGY, 32 Welbeck Street, London W1M 7PG (01–935 6867).

FRACTIONATION AND DOSE-RATE RELATIONSHIPS: FORMULÆ, EXPERIMENTS AND CLINICAL EXPERIENCE

By W. E. Liversage

St. Bartholomew's Hospital, London

On changing from a low dose-rate irradiation to a fractionated high dose-rate irradiation, the equivalent total dose may be found by applying the CRE system of Kirk *et al.* (1971; 1972; 1973; 1975a; 1975b), the general formula of Liversage (1969), combined with the equivalent single skin dose formula of Liversage (1971) or the TDF system of Orton and Ellis (1973) and Orton (1974).

Experiments on pig-skin by Turesson (1979), in which geometric conditions were kept constant, show that the CRE system of Kirk *et al.*, over-estimates the required dose by 40%, the system of Liversage predicts the required dose to an accuracy of ±10% and the TDF system of Orton and Ellis underestimates the the required dose by approximately 20%.

An analysis of the equivalent doses found from clinical experience by eight radiotherapists when treating carcinoma of the cervix, shows that when using the normalizing constants recommended by their authors, these three systems on average over-estimate the required dose at high dose-rate by 82%, 30% and 11% respectively (Liversage, 1978).

Turesson, from her pig-skin experiments, has established new normalizing constants for both the TDF and CRE systems. If these normalizing constants are employed instead of those recommended by the authors, all three systems predict that the given dose at high dose-rate should be 30% higher than that found by clinical experience.

The discrepancy between the pig-skin experiments of Turesson and the clinical experience of radiotherapists treating carcinoma of the cervix, may be due to the fact that different tissues behave differently and/or to the fact that sources tend to move away from the vaginal epithelium during low dose-rate treatment, thus delivering a lower dose than prescribed. During high dose-rate treatment, no such movement occurs and the prescribed dose is truly delivered.

REFERENCES

KIRK, J., GRAY, W. M. and WATSON, E. R., 1971. Cumulative radiation effect. Part I. Fractionated treatment regimes. *Clinical Radiology*, *22*, 145–155.

1972. Cumulative radiation effect. Part II. Continuous radiation therapy—long-lived sources. *Clinical Radiology*, *23*, 93–105.

1973. Cumulative radiation effect. Part III. Continuous radiation therapy—short-lived sources. *Clinical Radiology*, *24*, 1–11.

1975a. Cumulative radiation effect. Part IV. Normalization of fractionated and continuous therapy—area and volume correction factors. *Clinical Radiotherapy*, *26*, 77–88.

1975b. Cumulative radiation effect. Part V. Time gaps in treatment regimes. *Clinical Radiology*, *26*, 159–176.

Liversage, W. E., 1969. A general formula for equating protracted and acute regimes of radiation. *British Journal of Radiology*, *42*, 432–440.

1971. A critical look at the ret. *British Journal of Radiology*, *44*, 91–100.

1979. A comparison of the predictions of the CRE, TDF and Liversage formulae with clinical experience. *High dose-rate afterloading in the treatment of cancer of the uterus.* Report of an International Workshop held at the Middlesex Hospital Medical School, London, April 1978. *The Britihs Journal of Radiology*, *Special Report 17* (in press).

Orton, C. G., 1974. Time-dose factors (TDFs) in brachytherapy. *British Journal of Radiology*, *47*, 603–607.

Orton, C. G. and Ellis, F., 1973. A simplification in the use of the NSD concept in practical radiotherapy. *British Journal of Radiology*, *46*, 529–537.

Turesson, I., 1978. Fractionation and dose rate in radiotherapy. An experimental and clinical study of cumulative radiation effect. M.D. thesis, University of Goteborg, Sweden.

PRE-OPERATIVE IRRADIATION OF UTERINE CANCER USING THE CATHETRON

By D. O'Connell and N. Howard

Radiotherapy Department, Charing Cross Hospital

and M. G. R. Hull

Department of Gynaecology and Obstetrics
Bristol Maternity Hospital

This paper is an investigation into the relative effectivity of high and low dose-rate intracavitary irradiation in early carcinoma of the uterus, both body and cervix. It is concluded that:

1. As regards local extirpation of growth, the affects are equal in carcinoma of the cervix, but high dose-rate irradiation is very much more effective in carcinoma of the body.
2. Major morbidity is more likely to follow radiation with radium low dose-rate sources than with high dose-rate sources, probably due to the fixed geometry of the latter, which are inserted for periods of minutes. In this trial the low dose-rate sources were left in for a period of 48 hours.
3. It was found possible to give the treatment with the high dose-rate sources without anaesthetic and as an outpatient.

Erratum

The legend to Fig. 6 of the article Dosimetry of cathetron applicators in intracavitary therapy, The British Journal of Radiology, *51*, p.513 appeared incorrectly. The legend should read:

Isodose distributions normalized at point A for Manchester and Cathetron loadings given in Fig. 3. (A) equal periods of exposure of uterine and ovoid catheters. (B) ovoid catheter contribution increased by 12.5% to make it proportional to Manchester ovoid activity.

Forthcoming events and other notices

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

NEW RADIOPHARMACEUTICALS INCLUDING ^{123}I

An all day meeting organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on Wednesday, February 14, 1979 at the Middlesex Hospital Medical School.

Further information and registration from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

IMAGING IN NUCLEAR MEDICINE

An evening meeting to be held on Thursday, February 15, 1979 at The British Institute of Radiology, 32 Welbeck Street, London, W1, organized jointly by The British Institute of Radiology, the Royal College of Radiologists and the Royal Society of Medicine (Section of Radiology).

Further information contact the General Secretary, The British Institute of Radiology.

WORKSHOP ON THE USE OF COMPUTERIZED TOMOGRAPHIC SCANNERS IN RADIOTHERAPY

Following the successful workshop meeting on "The Use of Computers in Radiotherapy in Europe", held at the International Atomic Energy Agency in July 1976, the Commission Informatique of the European Association of Radiology will hold a workshop on the "Use of Computerized Tomographic Scanners in Radiotherapy", at the headquarters of the World Health Organization on March 28–30, 1979.

The meeting is designed to promote discussions among therapeutic and diagnostic radiologists, physicists and computer experts with previous experience in this field and will be limited strictly to 150 participants.

The programme will include invited and proffered papers and discussions concerning the recognition and definition of tumour and target volumes and treatment planning as well as future directions for development. The proceedings will be published.

Further information can be obtained from the General Secretary, Professor R. J. Berry, Department of Oncology, The Middlesex Hospital Medical School, London W1P 7PN.

INTERNATIONAL SYMPOSIUM ON RADIOLOGY OF THE SMALL INTESTINE AND DUODENUM

As part of the post-graduate teaching programme organized by the C.E.P.U.R. (Section of digestive radiology: Prof. P. Bodart), on March 30–31, 1979 in Brussels (Louvain-en-Woluwe), Belgium, there will be an international symposium on the subject of radiology of the small intestine and duodenum.

Preliminary scientific programme: techniques of examination including angiography; benign and malignant tumours; Crohn disease; other inflammatory diseases; vascular disorders; diffuse enteropathies.

Information and registration: Prof. J. Pringot, Service of Radiology, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Bruxelles.

RADIOBIOLOGY MEETING

The following meeting is scheduled at the Institute: "Preview of papers for the International Congress, Japan". April 20, 1979. This will be a general meeting, and proffered papers are invited. Titles and preferably brief abstracts of papers should reach Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX, by March 15, 1979.

Further information can be obtained from the General Secretary, The British Institute of Radiology (01–935 6237).

1979 THE BRITISH INSTITUTE OF RADIOLOGY ANNUAL CONGRESS

The 37th British Institute of Radiology Annual Congress and Scientific Exhibition will be held at the Middlesex Hospital Medical School on April 26–27, 1979. Included in a programme of invited papers on diagnosis, therapy, radiological physics and nuclear medicine topics will be the Presidential Address by Mr. W. M. Ross entitled *The Institute, yesterday and tomorrow*, and the Silvanus Thompson Memorial Lecture by Professor G. E. Adams on *Past, present and future of hypoxic cell sensitizers*.

Details and registration from The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

BRITISH ASSOCIATION OF CLINICAL ANATOMISTS

This new Association was founded in 1977 to strengthen the ties between medical/dental science anatomists and clinicians in all branches of medicine, and to promote the subject of clinical anatomy with respect to both teaching and research and to the evaluation of normal structure and function. The Association plans to hold two meetings a year, and the Summer Meeting for 1979 will be held at the University of Manchester on May 11; the deadline for abstracts will be March 3.

Further details about membership and the meeting may be obtained from the Secretary, Professor R. M. H. McMinn, Royal College of Surgeons, 35–43 Lincoln's Inn Fields, London WC2A 3PN.

FUNDAMENTALS IN TECHNICAL PROGRESS IN ULTRASOUND, DOSE PLANNING AND DATA PROCESSING IN NUCLEAR MEDICINE

An International Symposium to be held at the University of Liège (Sart-Tilman) on May 11–12, 1979. It will include invited papers by universities specialists and manufacture engineers, tending to present an approach of a concerted plan for developments in the near future.

Further information from Dr. J. Garsou, Agrégé, Contrôle Physique Radiations, Radiothérapie, 59 Boulevard de la Constitution, B-4020 Liège.

INTERNATIONAL SYMPOSIUM ON PERCUTANEOUS BIOPSY AND THERAPEUTIC VASCULAR OCCLUSION

To be held May 7–9, 1979 in Munich. Topics of biopsy: bone, lung, mediastinum, pancreas, kidney, liver, lymph-nodes, mammary gland. Topics of vascular occlusion: G.I. tract, lung, liver, kidney, cervicofacial, cerebromedullary, gynecologic, traumatic and pathologic bleeding.

Application and information: Prof. Dr. H. Anacker, Institut für Röntgendiagnostik der Technischen Universität, Klinikum r.d.I., Ismaningerstr. 22, D-8000 München 80.

THIRD EUROPEAN NUCLEAR MEDICINE SOCIETY MEETING

This meeting will be held in Karlovy Vary, Czechoslovakia, May 15–18, 1979 and is organized by the Czechoslovak Society of Nuclear Medicine and Radiation Hygiene.

The official languages will be English, French, German and Russian and simultaneous interpretation will be provided.

Registration: Czechoslovak Medical Society, J. E. Purkyne, 3rd European Congress of Nuclear Medicine, Sokolská 21, 120 26 Praha 2, Czechoslovakia.

Mackenzie Davidson Memorial Lecture

To be given by Dr. G. B. Schofield, Medical Officer, British Nuclear Fuels Ltd., on *Biological control in a plutonium production facility* at The British Institute of Radiology, 32 Welbeck Street, London, W1 on Thursday, May 17, 1979.

International Symposium on Interventional Radiology

An E.A.R. Symposium, organized by the Portuguese Society of Radiology and Nuclear Medicine, will be held May 30–June 2, 1979 in the Algarve, Portugal.

Proposed sessions include vascular therapy; selective embolization and management; catheter implantation in chemotherapy and percutaneous treatments; ultrasonic guiding techniques and nuclear imaging as a guiding technique for biopsy and fluid aspiration.

For further information contact the Portuguese Society of Radiology and Nuclear Medicine, 123, 1.° Esq., Avenida Elias Garcia, Lisbon 1, Portugal.

Nuclear Cardiology

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on June 20, 1979 at the Institute House.

Further information contact the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

IV European Congress of Radiology

The IV European Congress of Radiology will take place in Hamburg (German Federal Republic), September 4–8, 1979.

Scientific programme:

diagnostic research of organs of the upper abdomen;

diagnostic research in nuclear medicine: organs of the upper abdomen;

radiotherapy in tumours of the genital system of males and females;

radiobiology and X-ray protection (combined therapies and risks of ray exposure);

radiophysics and techniques (methodical problems in diagnostics and in planning of radiotherapy).

Enquiries: Secretary of the IV European Congress of Radiology, Postfach 10 64 07, D-2000 Hamburg 1, Federal German Republic.

Quantitation of Tumour Response: a Critical Appraisal

The L. H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to simulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.

Factors of prognostic significance.

In vitro assays of tumours excised after treatment *in vivo*.

The choice of suitable experimental models in rodents.

The role of human tumour xenografts.

Statistical evaluation of tumour response data.

The limitations and artefacts of each assay technique.

The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

Symposium on Diagnostic Radiology

Sponsored by the Department of Radiology, University of Connecticut and the Faculty of Radiologists of Ireland a symposium to be held in Killarney, Ireland, September 15–21, 1979.

An international faculty of leaders in the field of radiology from the United States, Great Britain and Ireland will discuss recent advances, CT scanning and ultrasound of the major organ systems.

Further details may be obtained from Dr. D. B. Crawford, Department of Radiology, University of Connecticut Health Center, Farmington, CT 06032, USA.

XII Symposium Neuroradiologicum

The XII Symposium Neuroradiologicum will be held in Washington, District of Columbia, October 10–16, 1982. The first Symposium was held in Antwerp, Belgium, in 1939 and only once before has a Symposium Neuroradiologicum been held in the United States (New York City, 1964). Dr. Giovanni Di Chiro of Bethesda, Maryland, has been chosen to be the President of the Symposium. Vice President is Dr. Hillier L. Baker of Rochester, Minnesota, and Secretary General is Dr. David O. Davis of Washington, D.C.

Symposium on Spine and its Contents

E.A.R. "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in the:

(a) Equipments and investigative methods of spine and spinal cord.

(b) Radioanatomy and physiology of spine and spinal cord.

(c) Radiodiagnosis of pathological conditions.

(d) Interventive (diapeutic) radiodiagnostic methods.

For further information contact (not later than June 1979): The secretariate of "Vertebro 1980", P.O.B. 88, Sokolská 31, 120 26 Praha 2, Czechoslovakia.

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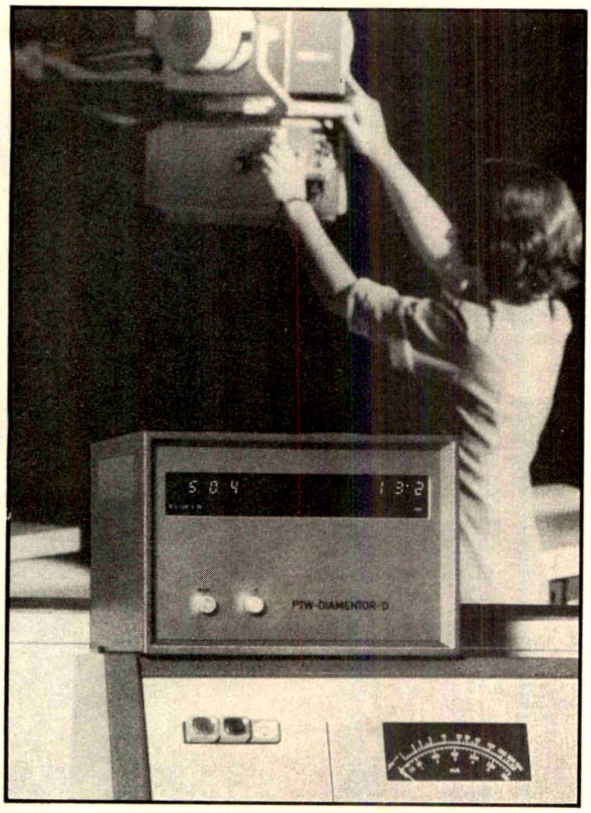

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Applications on the prescribed form close with the undersigned on 30th April, 1979, and further details, if required, are available from the Director of Medical Services, (Dr. L. N. Walsh).

(**Note:** Dr. Harold Fabrikant, Deputy Director of Radiology at Prince Henry's Hospital, is currently working in the National Hospital, Queen Square, London, and is contactable at that hospital).

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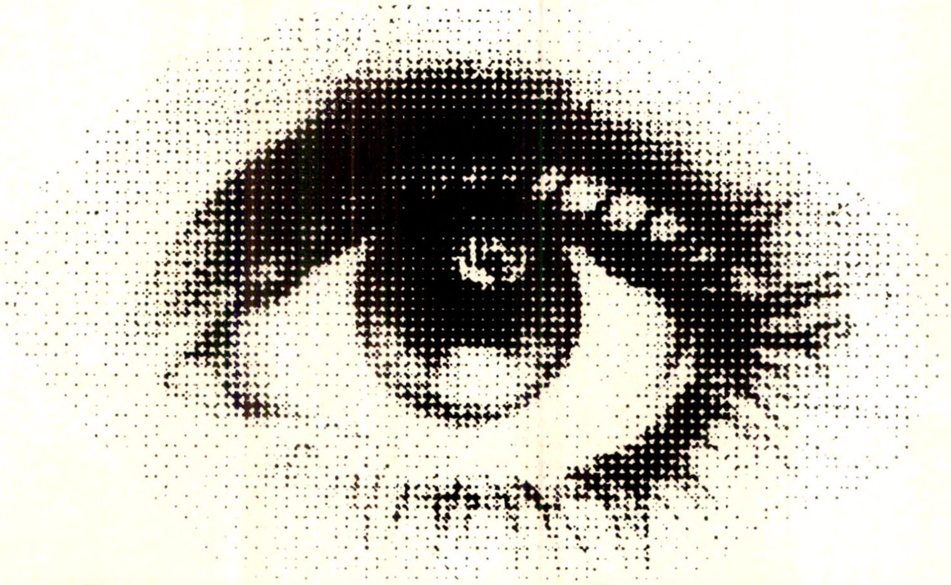

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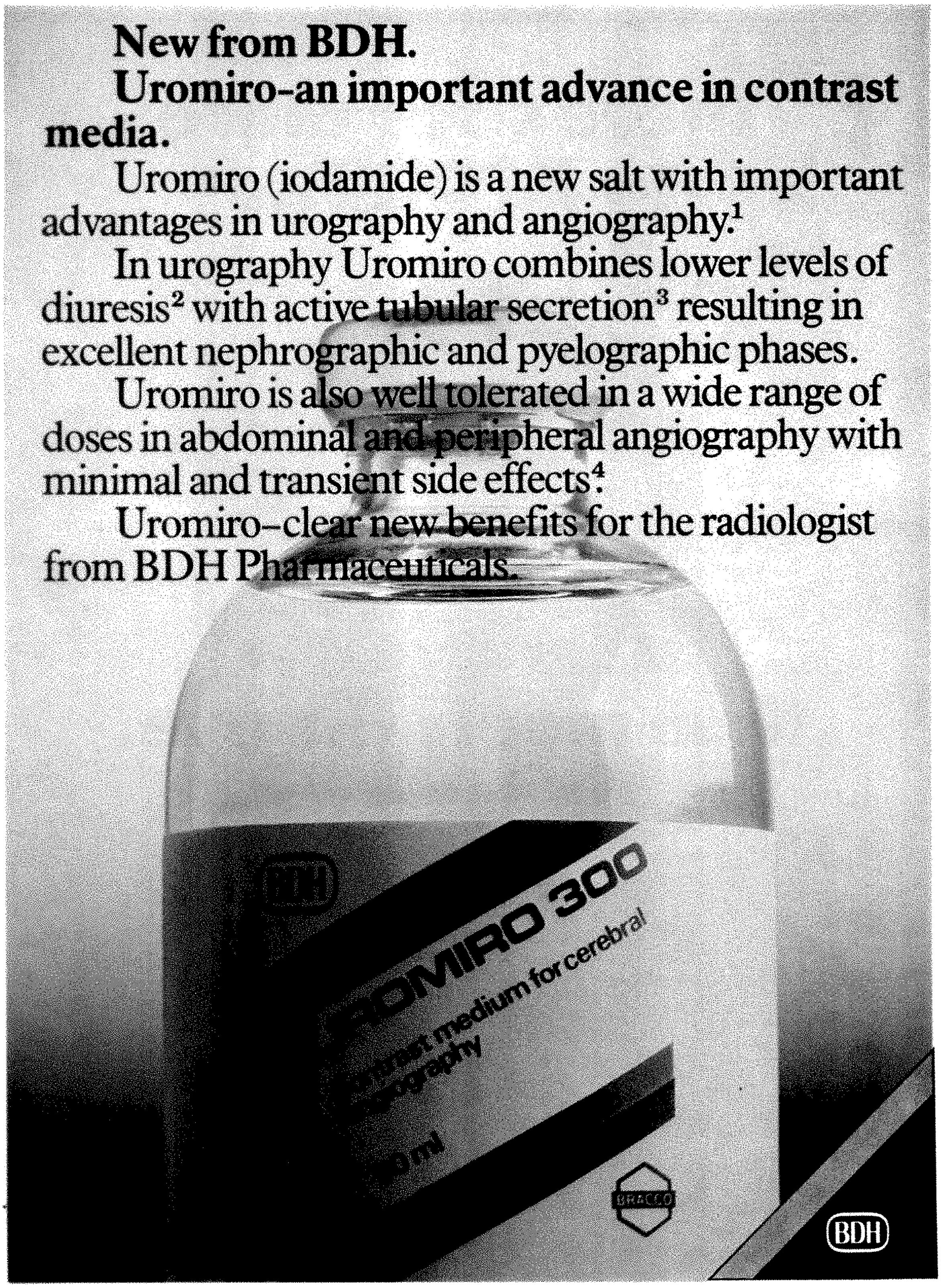

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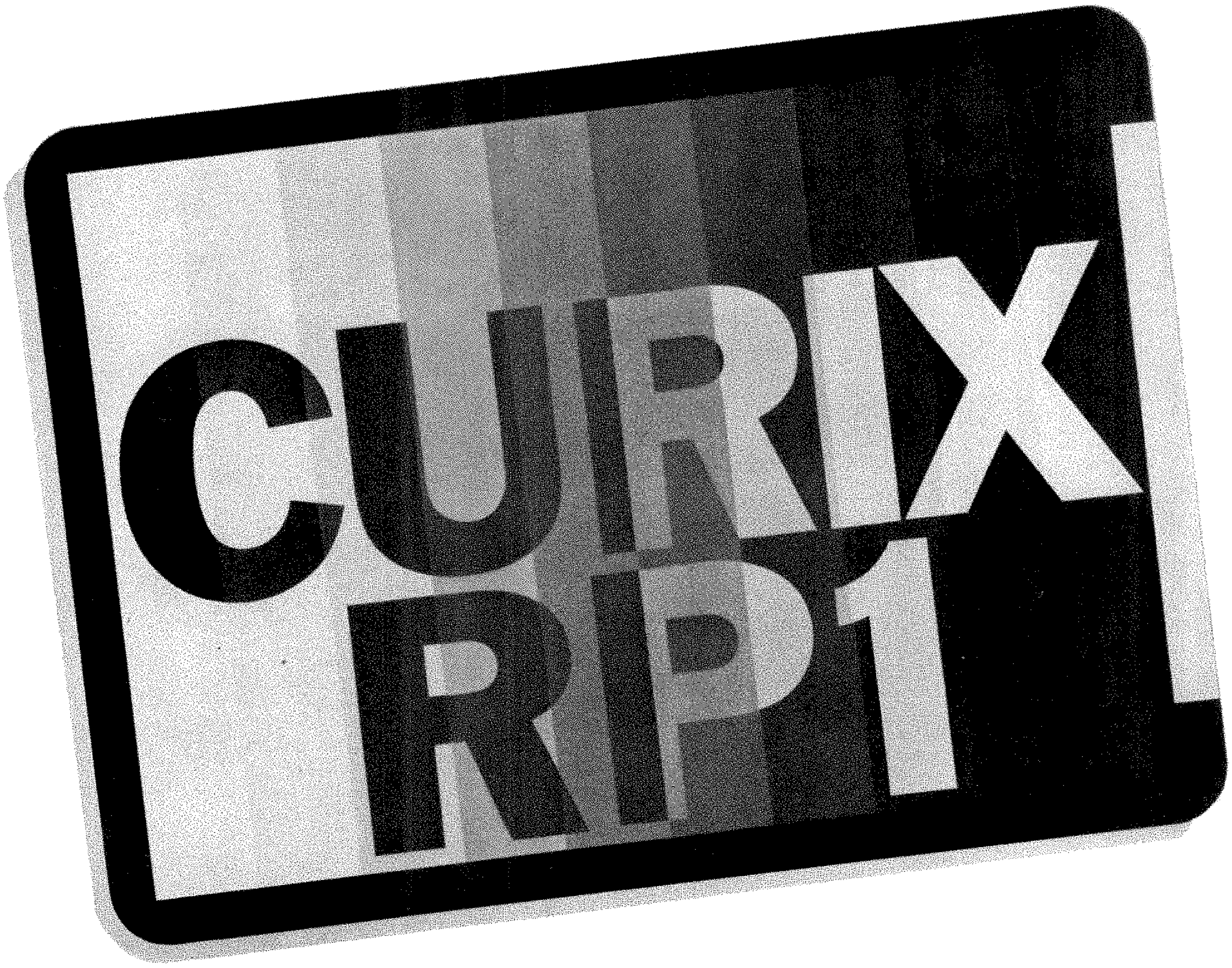

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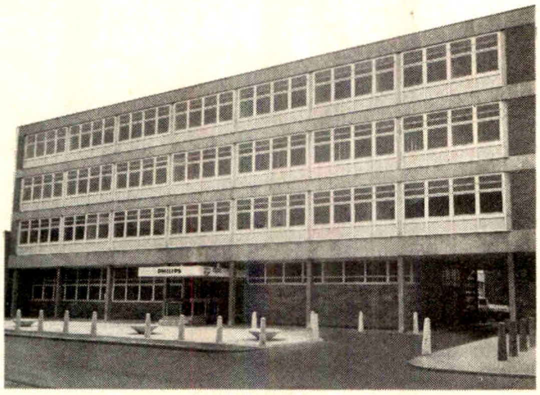

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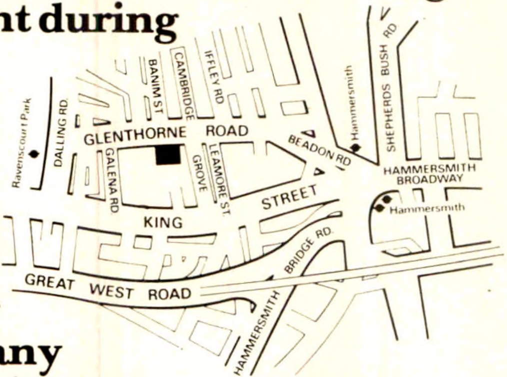

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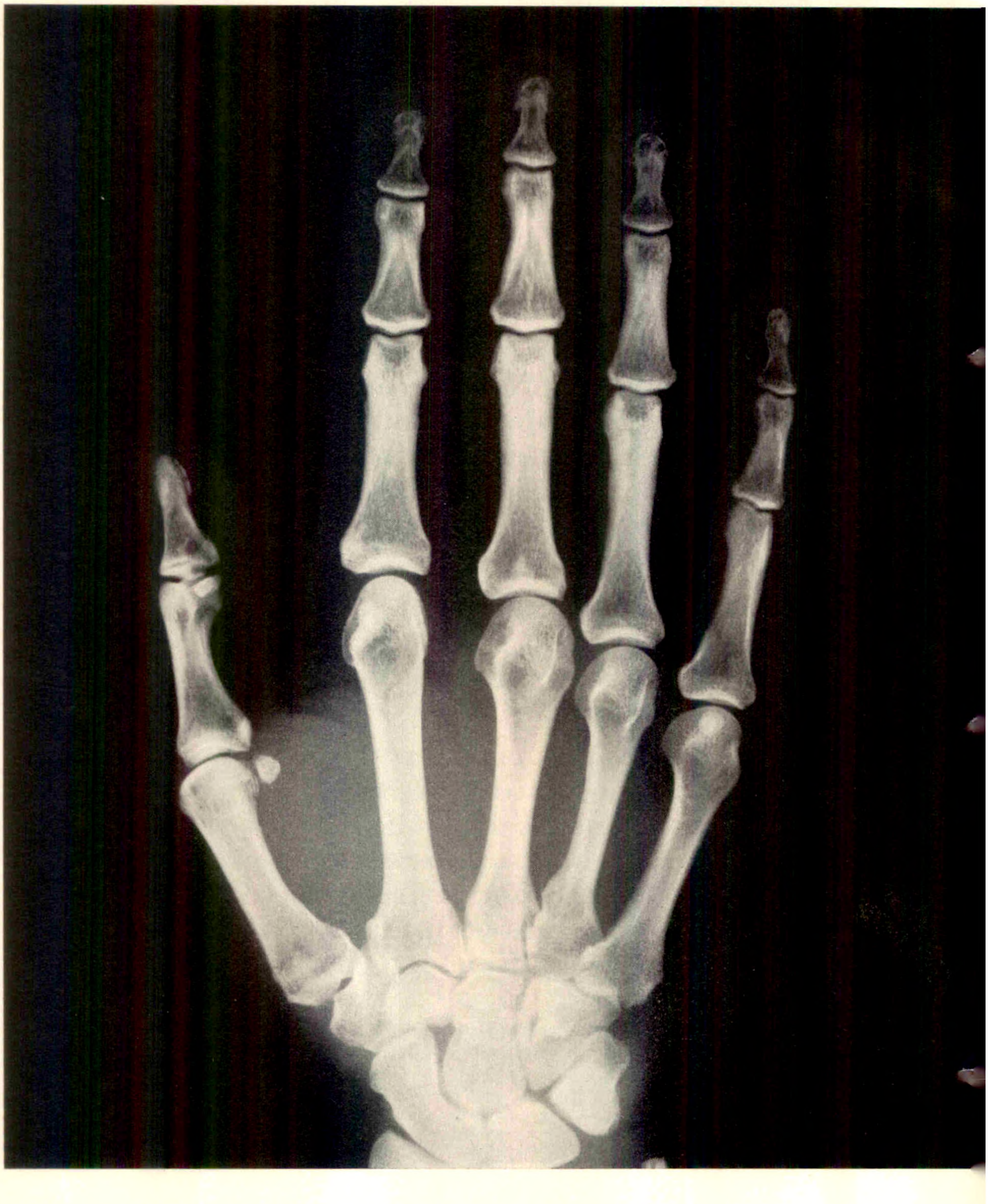

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Radiation Oncologist

Applications are invited for the post of Radiation Oncologist at the Ontario Cancer Foundation Kingston Clinic and the Department of Radiation Oncology of Queen's University at Kingston.

The new cancer clinic, which serves a population of 325,000 people in Eastern Ontario, occupies some 30,000 square feet of space and contains facilities for ambulatory patient care, radiation therapy (including both a 20 MeV linear accelerator and cobalt 60 beam therapy), teaching and research. Other support services include an independent medical records department, a treatment planning simulator, an A.E.C.L. TP–11 computer dedicated to treatment planning, a mould room, and an instrument shop. The research facility comprises about 1500 square feet of space for applied research in tumour biology and immunology. Appointments to the medical staff of the Clinic are made jointly by the Ontario Cancer Foundation and by Queen's University. A fully integrated undergraduate and graduate teaching programme has been developed and is being successfully maintained.

Further details regarding the appointment will be supplied on request. Applications with curriculum vitae and the names of three referees should be submitted to: Dr. Stewart Lott, Director, The Ontario Cancer Treatment and Research Foundation Kingston Clinic (Professor and Head, Department of Radiation Oncology, Queen's University), Kingston, Ontario, Canada K7L 2V7.

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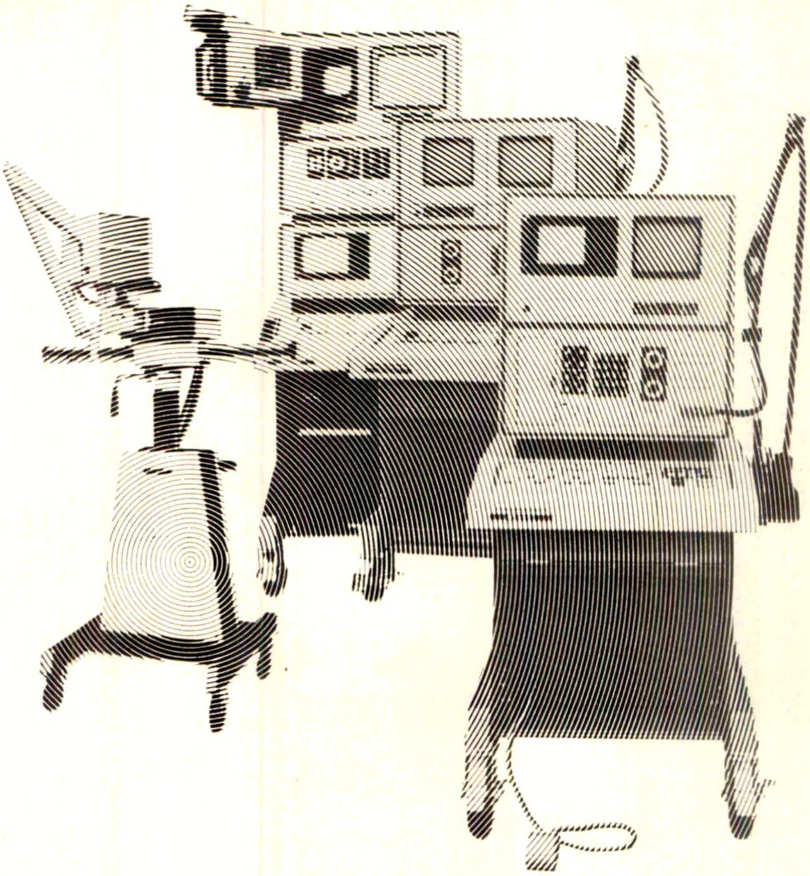

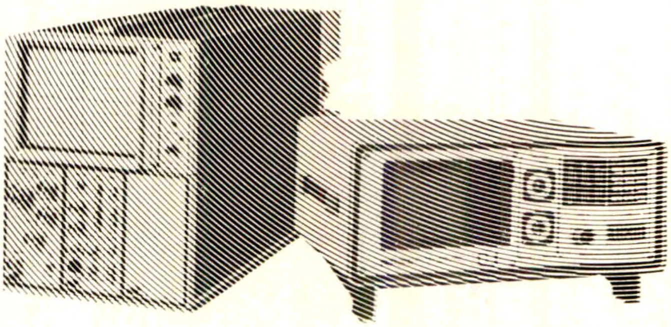

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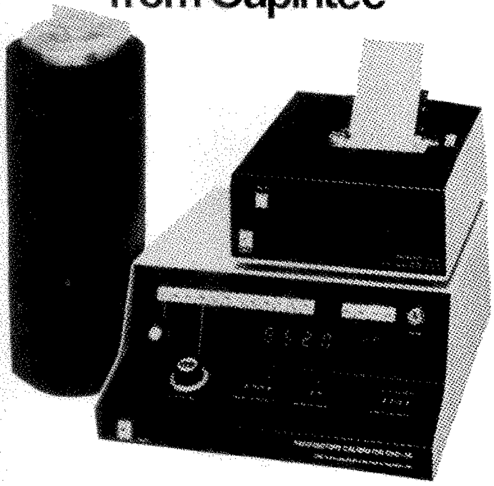

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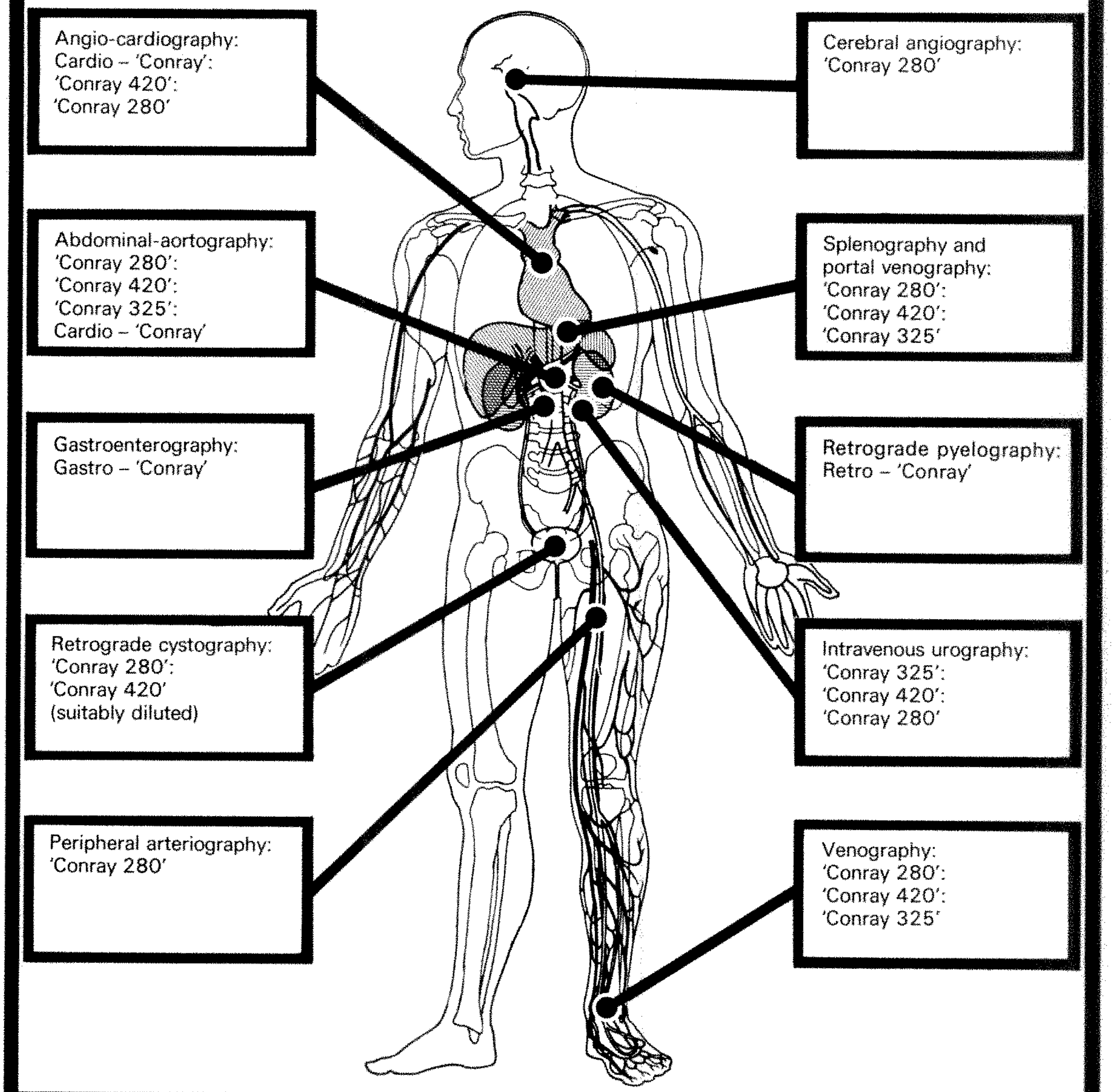

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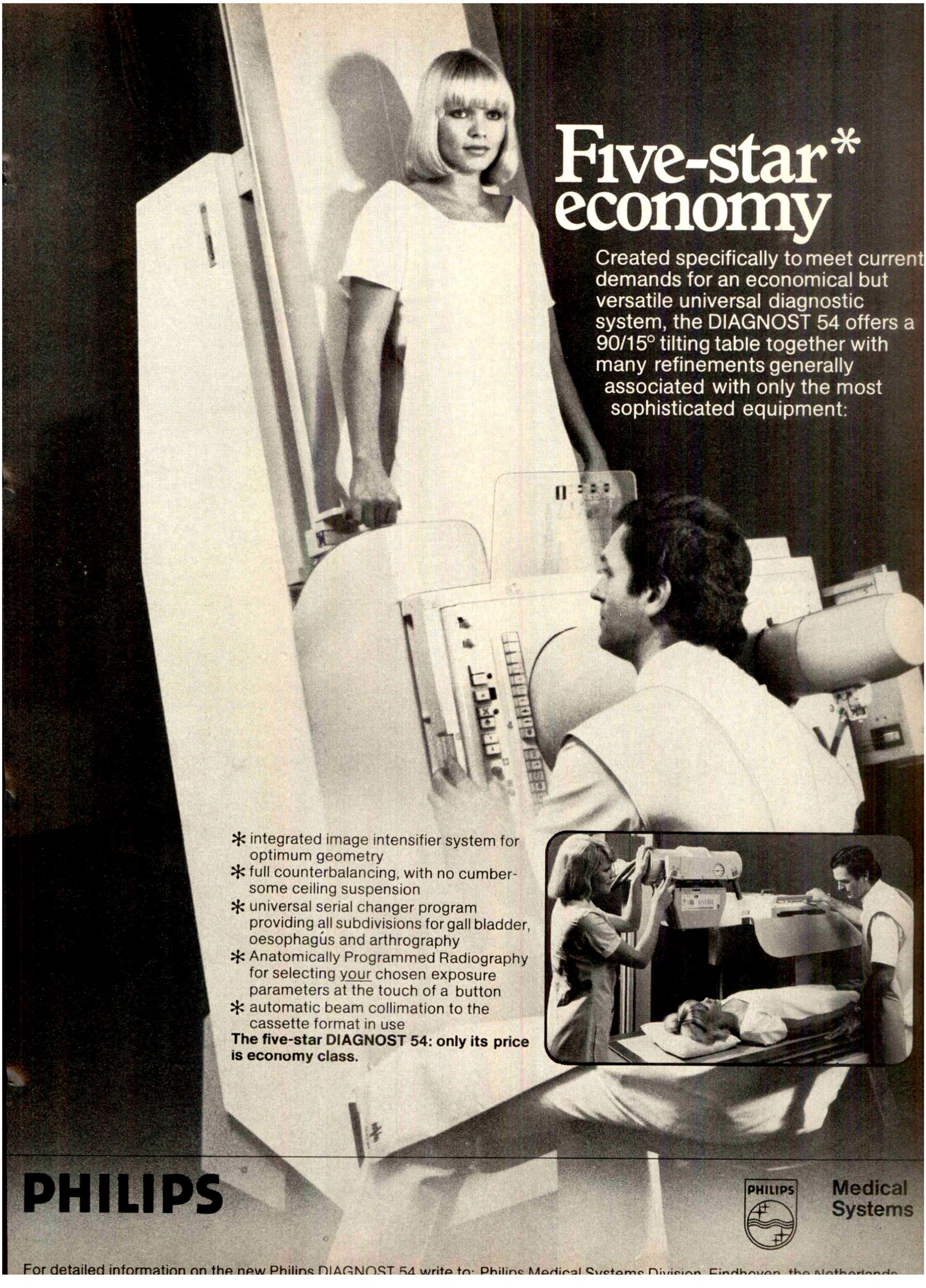

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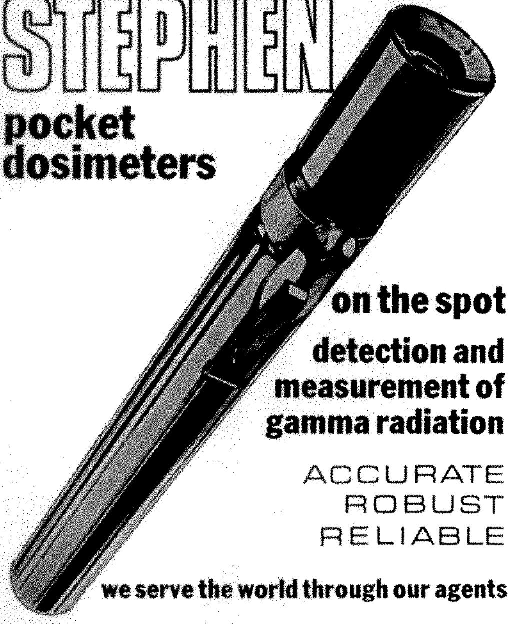

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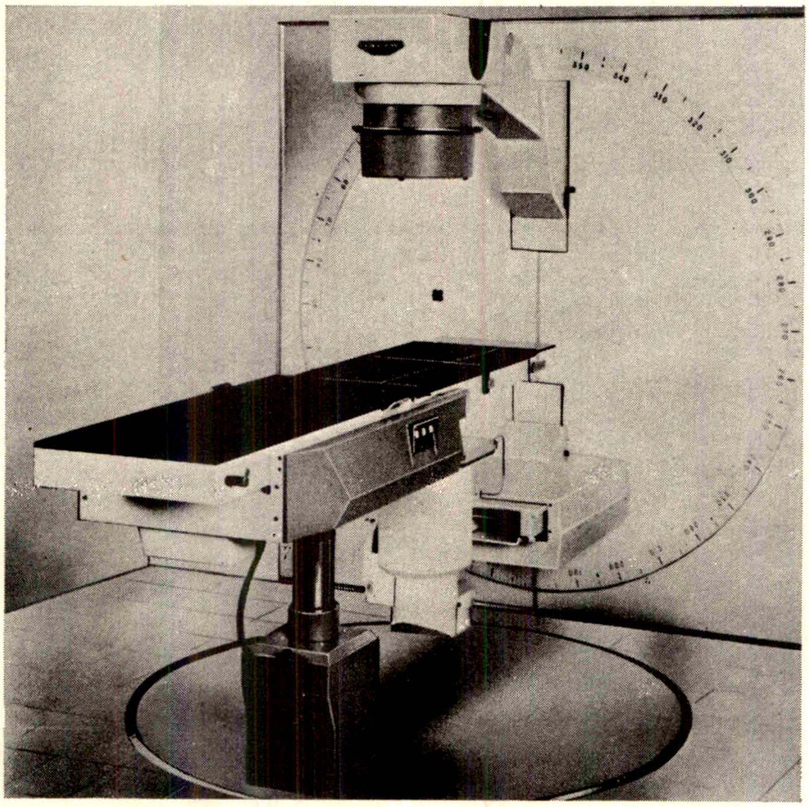

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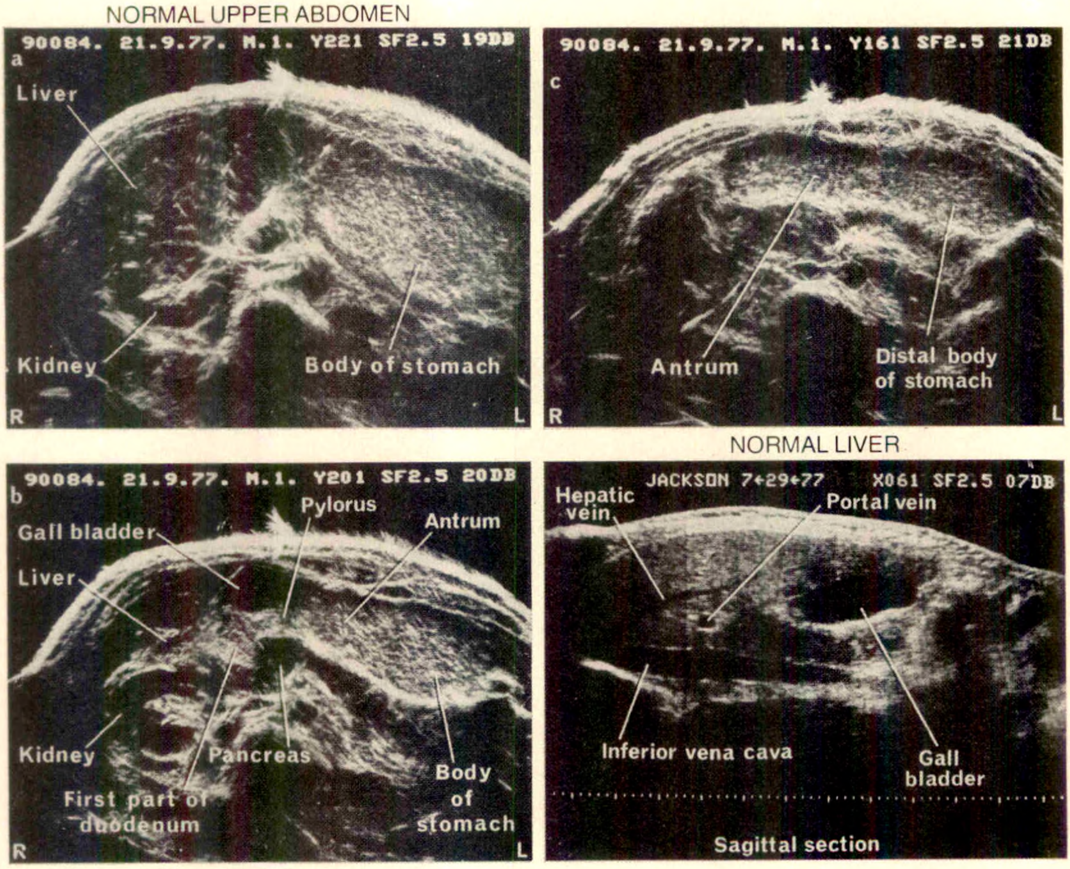

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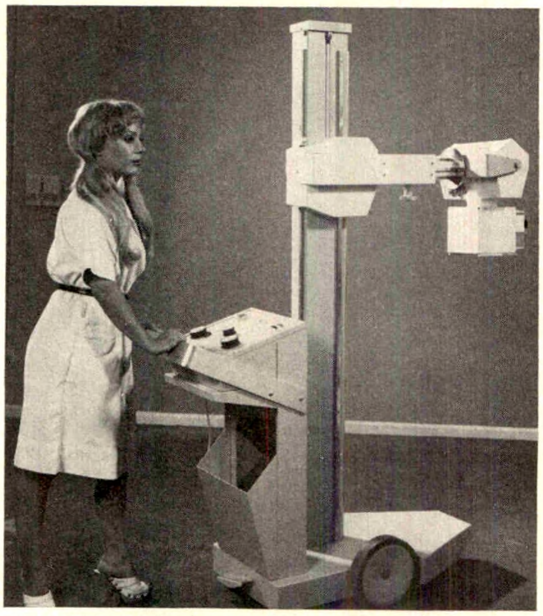

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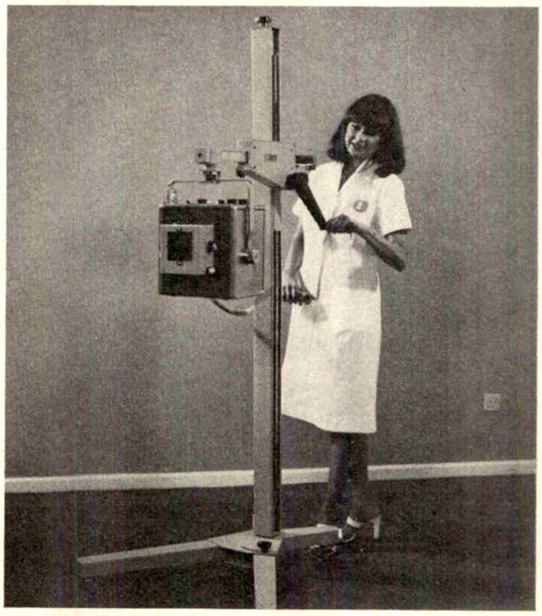

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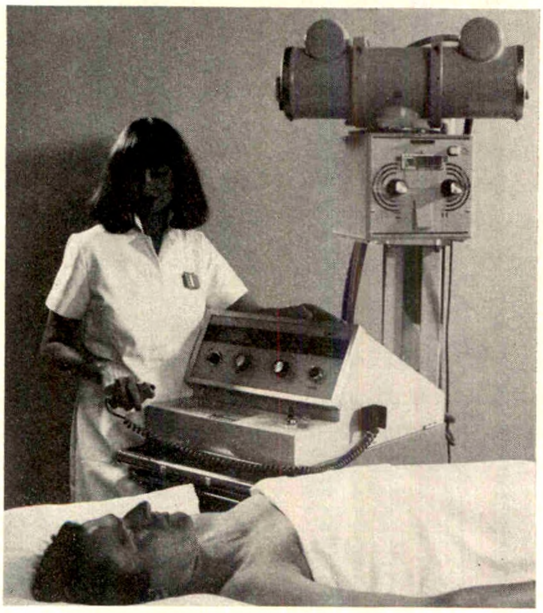

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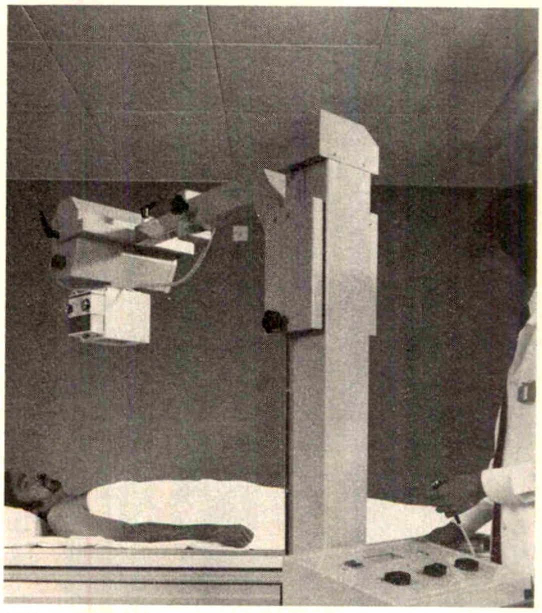

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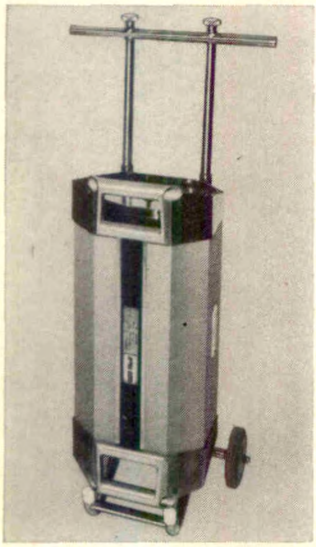

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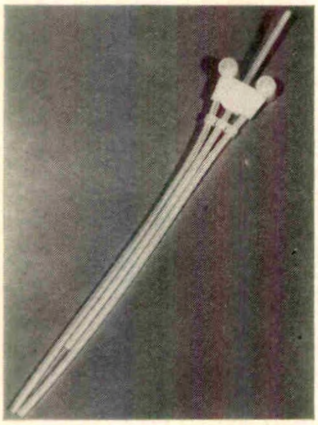

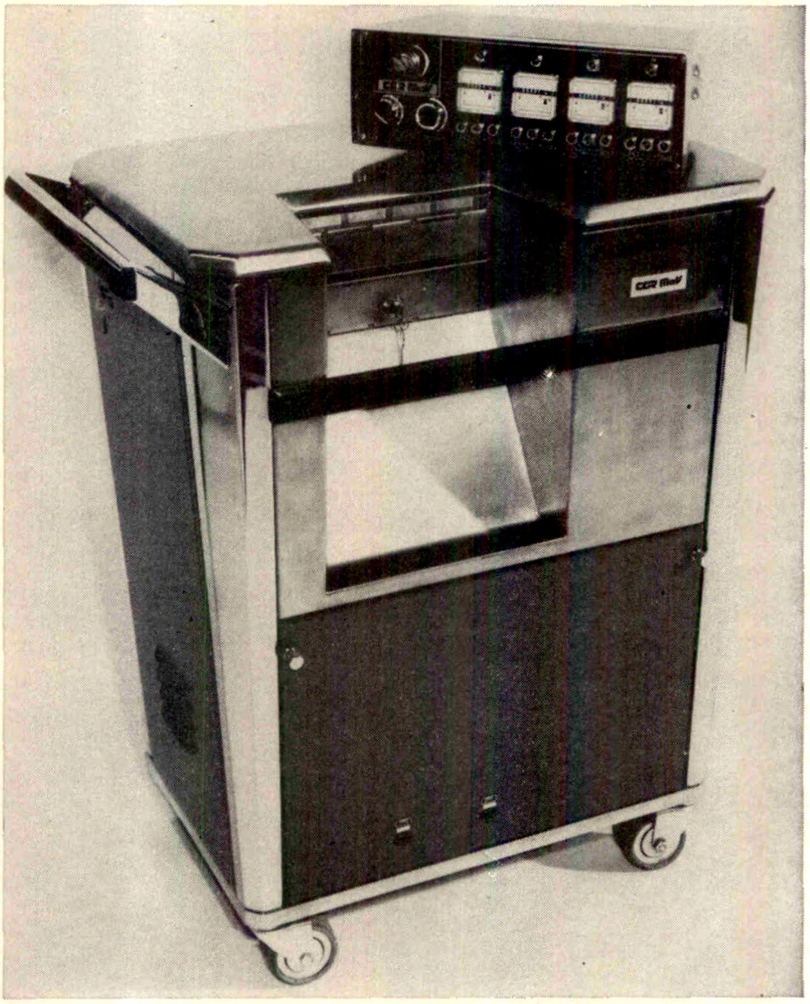

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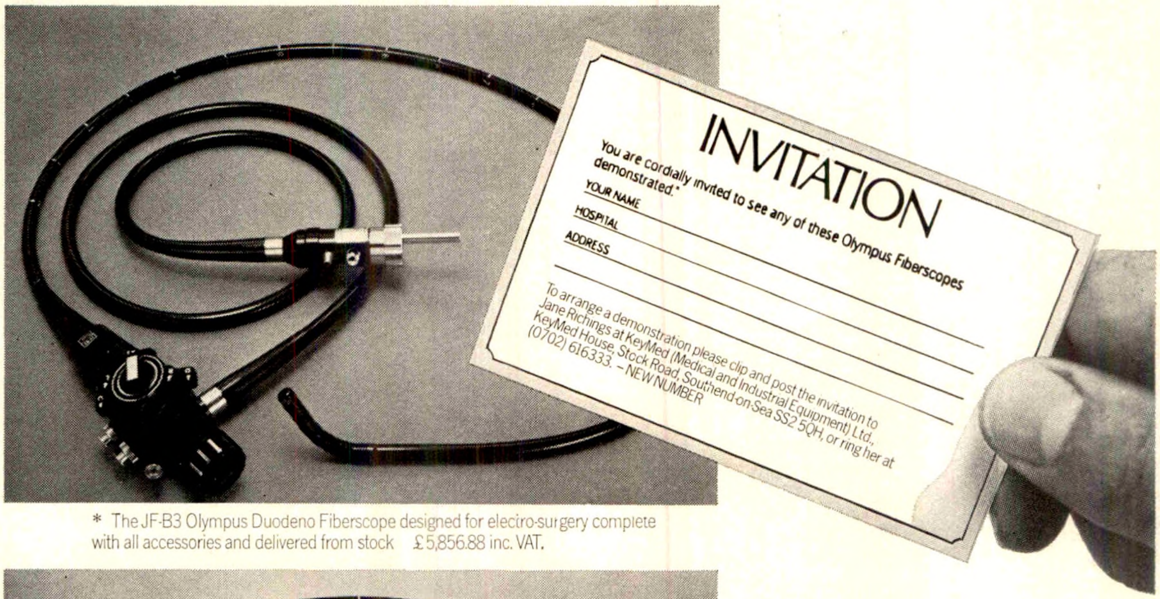

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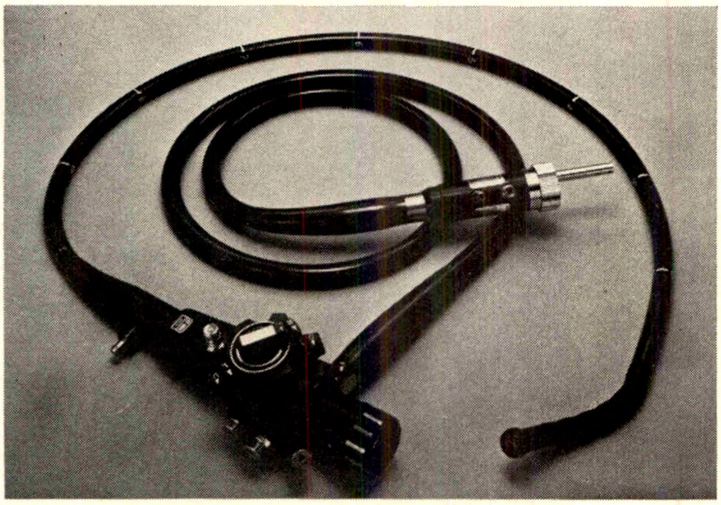

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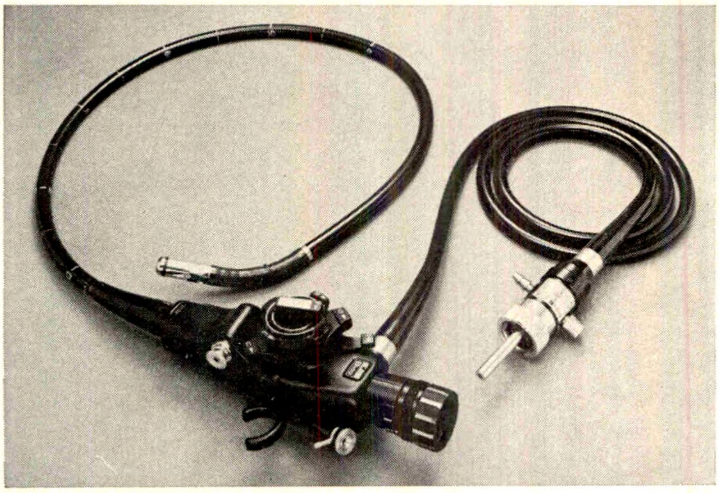

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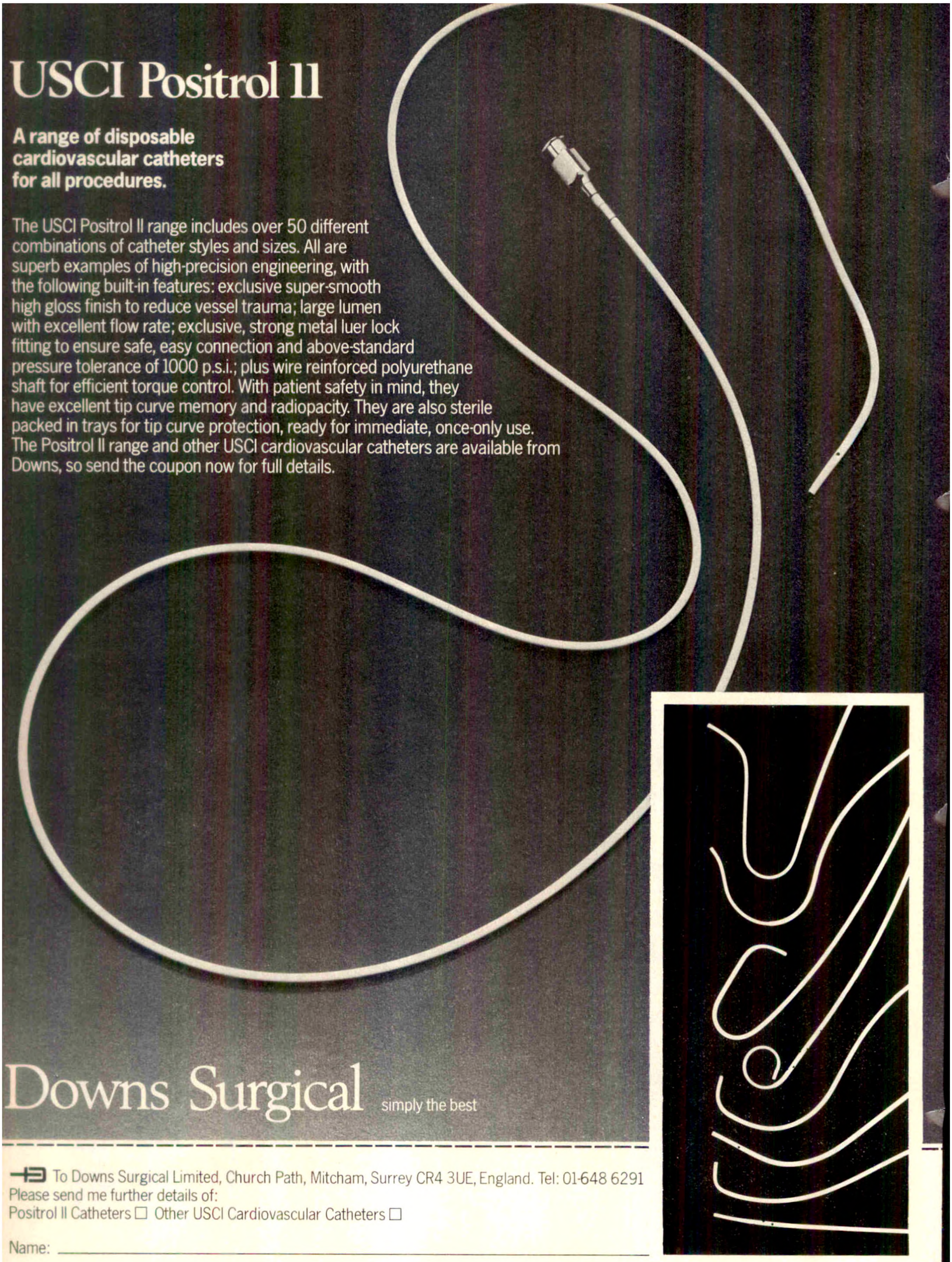

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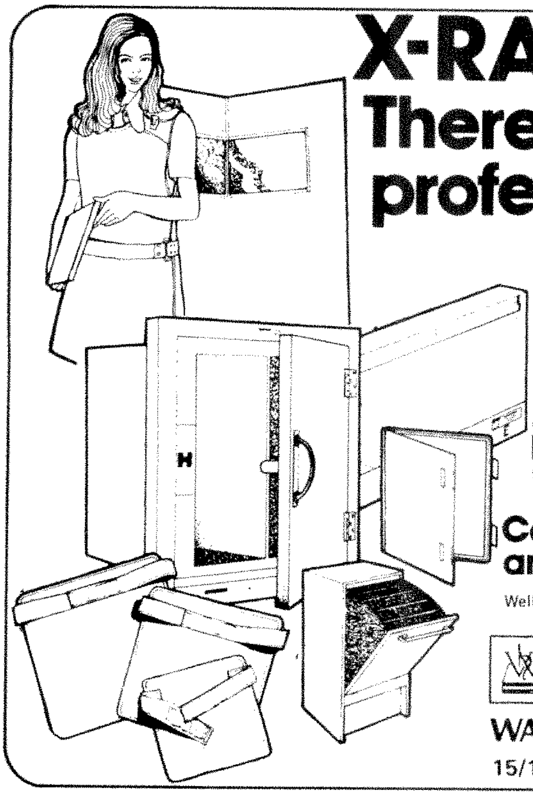

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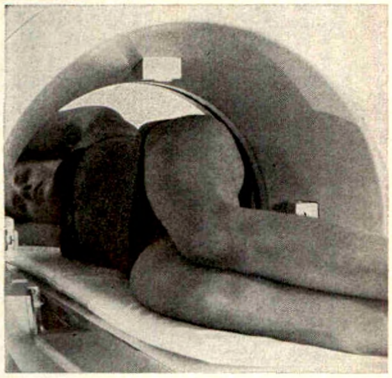

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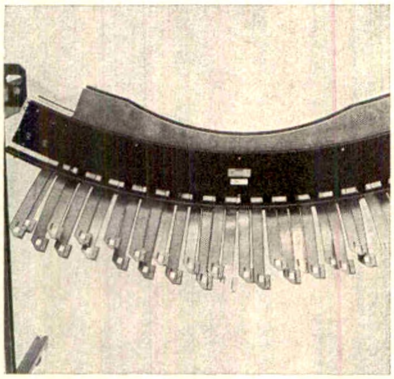

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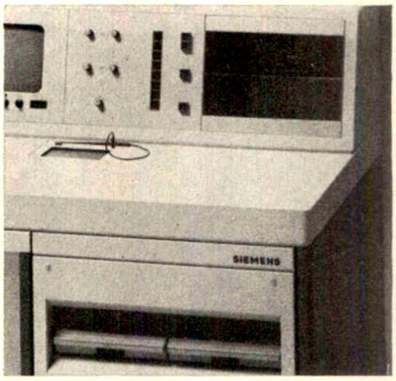

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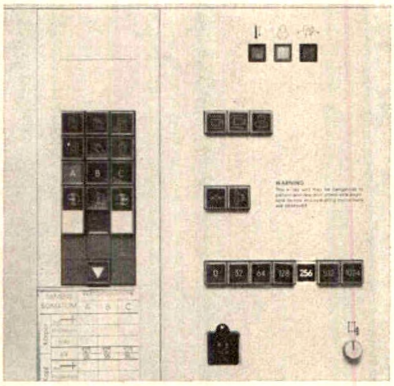

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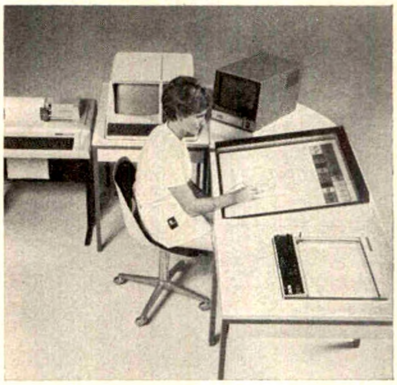

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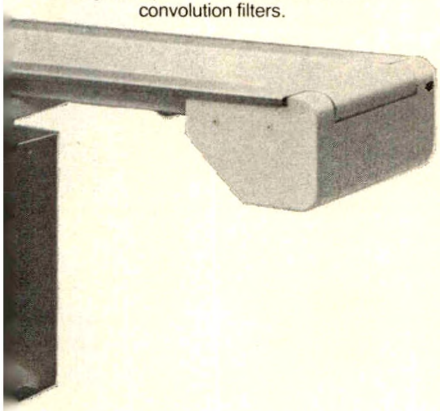

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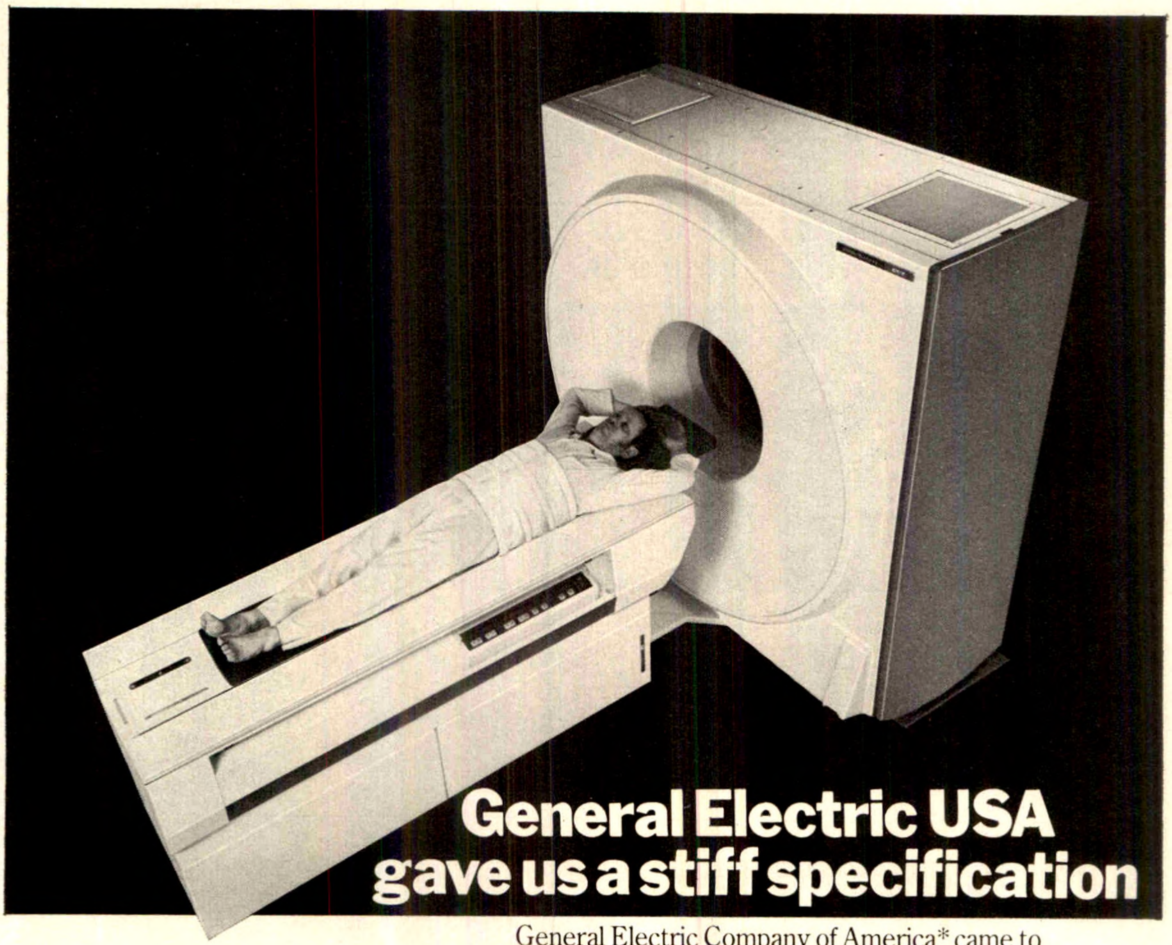

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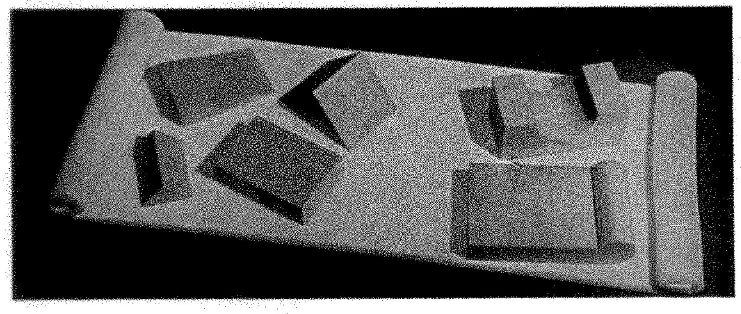

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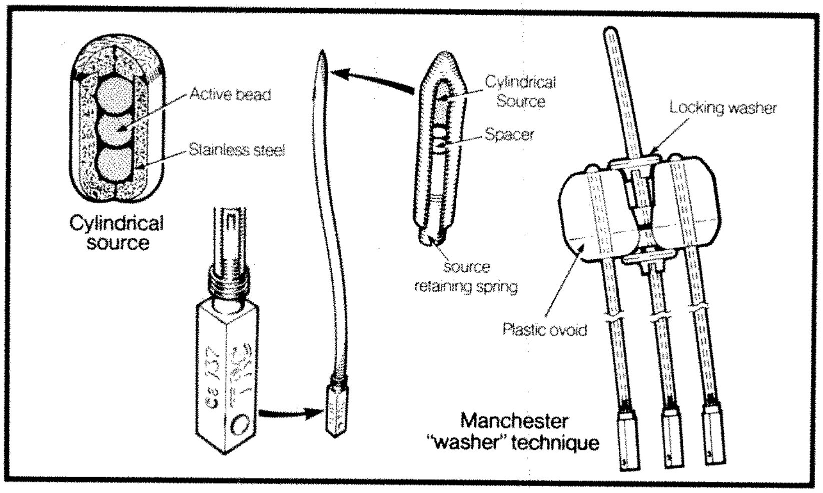

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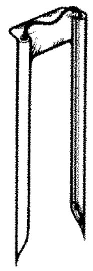

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1979, *British Journal of Radiology*, *52*, 169–172

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Ioxaglate, a new low osmolar contrast medium used in femoral angiography

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(*Received September, 1978*)

ABSTRACT

Ioxaglate, a new monoacid, dimeric contrast medium was compared with diatrizoate (Urografin 60%) in a series of 61 femoral angiographies. In a double blind group of 34 examinations all patients preferred ioxaglate which caused slight pain in only five cases, whereas after diatrizoate 14 patients felt severe pain (six were unable to keep their legs still) and 12 felt slight pain. Increase in heart rate and decrease in systolic and diastolic arterial blood pressure was seen after both contrast medium injections, but significantly less after ioxaglate than after diatrizoate.

A well known drawback of femoral angiography in arteriosclerotic patients is the pain caused by the injected contrast medium, sometimes provoking involuntary movements of the legs with resulting blurring of the films.

The pain is in part due to the hyperosmolarity of the commonly used contrast media (diatrizoate, metrizoate, iothalamate, ioxithalamate and others), and efforts have been made to develop contrast media with reduced osmotic activity. A dimeric and thereby less hypertonic contrast medium was used by Björk *et al.*, (1969) in a series of angiographies with significantly reduced subjective adverse effects compared to diatrizoate and metrizoate. The even less hypertonic, non-ionic medium metrizamide used by Almén *et al.*, (1977) gave excellent results producing no pain in femoral angiography in 20 patients.

Ioxaglate is a new dimeric contrast medium in which one of the acid groups has been replaced by a non dissociable amide (Fig. 1). In solution ioxaglate is therefore of low osmolarity. In the present investigation we studied the effects of ioxaglate used in femoral angiography compared with those of diatrizoate.

MATERIAL AND METHODS

From September 1977 to March 1978 a total of 61 consecutive femoral angiographies were performed by the Seldinger technique in 52 patients (Table I). In all angiographies at least two injections of contrast medium were given with the patient and catheter remaining in the same position. In one injection we gave ioxaglate, in the other diatrizoate (Urografin), the contrast medium generally used for angiography in our department. This enabled us to compare the reactions to both media in each patient.

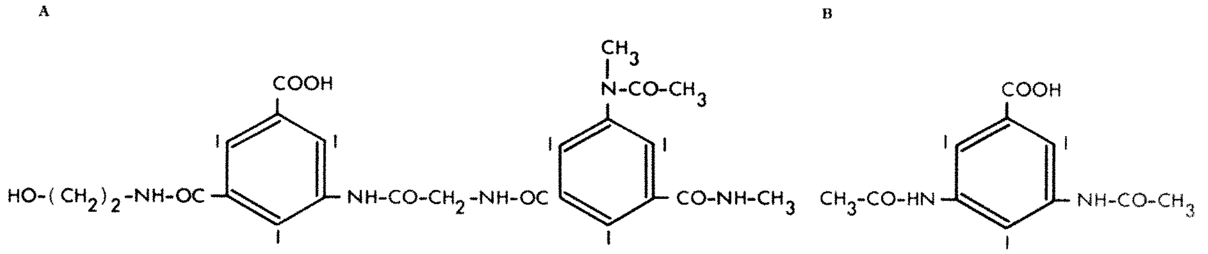

FIG. 1.

	A	B
Official name:	IOXAGLATE	DIATRIZOATE
Experimental or trade name:	A.G. 62–27	Urografin 60%
Iodine content	320 mg/ml	295 mg/ml
Osmolality, mol/kg water in solutions with 280 and 380 mg I/ml:	0.49 and 0.66	1.44 and 1.96
Number of iodine atoms/number of particles in solution:	6/2	3/2
Ratio meglumine/sodium salt:	2/1	6.6/1

The medium used first in each angiography was determined at random. The preparations employed were A.G. 62–27 and Urografin 60% (Fig. 1).

In 51 cases 40 ml of contrast medium were delivered in each injection in the abdominal aorta, 4–5 cm above the bifurcation, at the rate of 13 ml/sec. In the remaining ten cases the injections were made in the external iliac or the femoral artery of one or both sides. In these more peripheral angiographies proportionally lower doses of 10 to 20 ml were injected at the rate of 10 ml/sec. There was an interval of at least ten minutes between the two injections.

The spontaneous reactions of the patient to each injection were observed, and after each injection the patient was questioned about sensations of heat and pain. After completion of the two injections the patient was asked to state which of the injections had given the least discomfort. All observations and patient's complaints were registered in an individual case report.

Intra-arterial blood pressure and electrocardiogram were recorded from a few minutes before until four minutes after the injection. Since the blood pressure was measured through the angiographic catheter this pressure-recording was interrupted from a few seconds before until approximately 20 seconds after the injection.

The patients were not informed of the order in which the injections were given, this was known by the examining doctor in the first 27 angiographies, but not in the last 34 making this part of the trial double blind.

TABLE I

DISTRIBUTION OF AGE AND SEX IN 52 PATIENTS IN WHOM A TOTAL OF 61 FEMORAL ANGIOGRAPHIES WERE PERFORMED

	< 44 years	45–60 years	> 60 years	Total
Male	2	16	18	36
Female	0	3	13	16
Total	2	19	31	52

RESULTS

In the double blind part of the trial all patients stated that ioxaglate had given the least discomfort. The spontaneous reactions and indicated sensations of pain and heat after the two injections in this group are given in Fig. 2. Fourteen patients complained of severe pain after injection of diatrizoate, six were unable to keep their legs still, and hence blurring of films occurred. After ioxaglate no statement of severe pain was given. Slight movement (mainly grimacing) was seen in three patients, two of

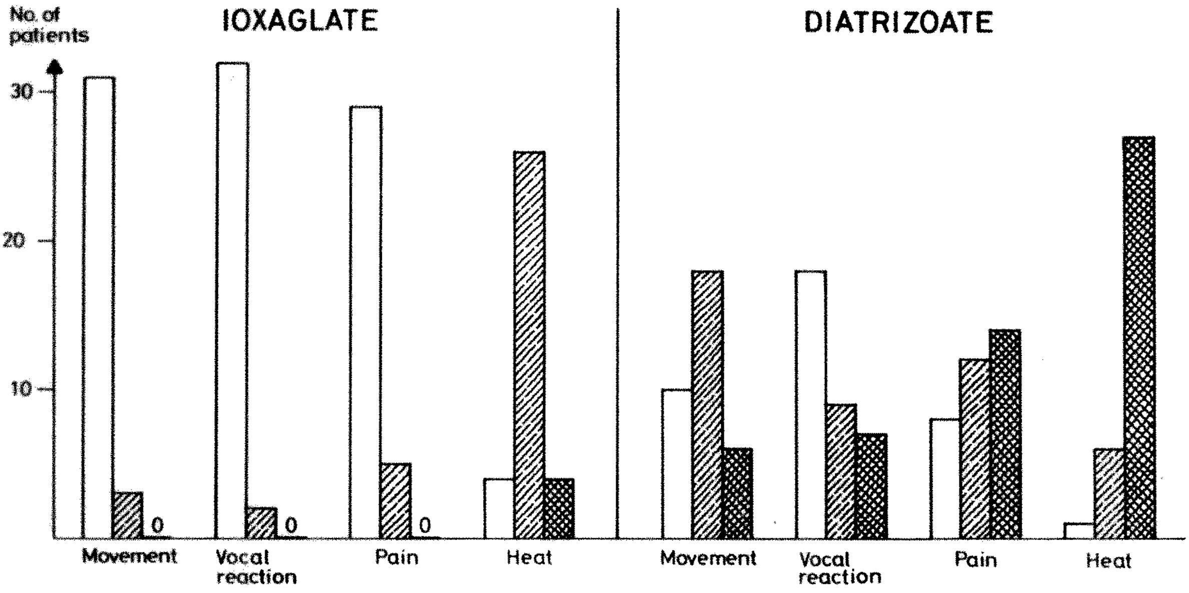

FIG. 2.

Reactions and sensations following injection of ioxaglate and diatrizoate in angiography in a double blind study comprising 34 examinations (28 aortic and six peripheral injections).

☐ None ▨ Light ▩ Severe

TABLE II

MEAN INCREASE IN HEART RATE (BEATS/MIN) AND DECREASE IN BLOOD PRESSURE (MM HG) AFTER INJECTION OF IOXAGLATE AND DIATRIZOATE IN A TOTAL MATERIAL OF 61 FEMORAL ANGIOGRAPHIES

Contrast medium	Ioxaglate			Diatrizoate		
Changes in	Heart rate	Systolic blood pressure	Diastolic blood pressure	Heart rate	Systolic blood pressure	Diastolic blood pressure
51 aortic injections	+5.4	−8.0	−6.1	+8.7	−26.1	−17.1
10 peripheral injections	+4.0	−19.4	−7.8	+7.9	−25.0	−10.0

whom described the injection as slightly painful. The difference between the number of patients feeling pain after injection of ioxaglate (five out of 34) and diatrizoate (26 out of 34) is highly significant (χ^2 test, $p < 0.001$).

The changes in heart rate and systolic and diastolic blood pressure appear in Table II. In most cases a slight decrease in heart rate was seen immediately after the injection followed by a more marked increase, generally accompanied by a decrease in blood pressure. In two cases the decrease in systolic blood pressure reached 60 mm Hg after injection of diatrizoate. The decrease was always less marked after ioxaglate than after diatrizoate. In some cases the only change in blood pressure after injection of ioxaglate was a slight increase, in a few cases the blood pressure did not change at all. Statistical analysis (Mann-Whitney rank sum test) of the haemodynamic effects of aortic injection of the two media showed significantly reduced changes after ioxaglate compared with diatrizoate (increase in heart rate, $p < 0.02$, decrease in systolic and diastolic blood pressure, $p < 0.001$). The changes after peripheral injection were smaller after ioxaglate than after diatrizoate, but the differences were not significant.

The results were apparently not influenced by the order in which the injections were given.

No difference in the radiographic properties of the two media could be observed.

A transient urticarial reaction with itching and periorbital oedema was observed in one patient 15 minutes after conclusion of an angiogram in which one injection of A.G. 62–27 and two of Urografin 60% had been given, each consisting of 40 ml. Two months later the patient underwent a new angiogram with identical injections without urticarial reaction.

DISCUSSION

The haemodynamic effects of intra-arterial injection of conventional contrast media and other hypertonic solutions are well described from animal experiments (Efsen and Munkner, 1968, Lindgren *et al.*, 1968, Read *et al.*, 1960) and clinical practice (Amundsen *et al.*, 1956, Boijsen *et al.*, 1971, Delius and Erikson, 1969). Hypertonic solutions have been found to produce a fall in peripheral vascular resistance resulting in increased blood flow and decreased arterial blood pressure, generally accompanied by increased heart rate. The decrease in blood pressure has been observed to reach maximum value 20–40 seconds after injection in the lower abdominal aorta in man.

The vascular reactions to angiography may be reduced by using a less hypertonic contrast medium. This was demonstrated in animal experiments by Almén and Trägårdh (1973) and in man by Almén *et al.* (1977) with the non-ionic contrast medium metrizamide. Their results are in accordance with the findings of the present study in which the vascular reactions were significantly reduced with the low-osmolar ioxaglate compared with the conventional medium diatrizoate.

All clinical reports support the hypothesis that the hypertonicity, relative to plasma, is at least in part responsible for the painful effect of the commonly used contrast media when injected intra-arterially. This effect is especially troublesome in hand angiography and, as in our material, in femoral angiography in severely arteriosclerotic patients.

Widrich *et al.* (1977) recommended intra-arterial administration of a local anaesthetic (lidocaine) prior to contrast medium injection during femoral angiography based on the finding of a distinct decrease in pain sensation in a controlled trial. They saw no side effects, but theoretically a new source of complications was added to the examination.

Conventional contrast media have in animal experiments been shown to exert an injurious effect on the vascular endothelium (Zinner and Gottlob, 1959). This effect is reduced when the low-osmolar contrast medium metrizamide is employed (Almén and Trägårdh, 1973) but no reduction may be expected by the injection of a local anaesthetic.

Conclusion

In order to reduce the pain associated with peripheral angiography we suggest that the conventional highly hypertonic contrast media be replaced by contrast media of low hypertonicity. Ioxaglate fulfilled our requirements as a contrast medium for use in femoral angiography in severely arteriosclerotic patients as it significantly reduced the pain and discomfort felt by the patients and enabled them to stay calm during the examination. Ioxaglate is delivered in stable watery solution, and is as easy to handle as the commonly used contrast media.

REFERENCES

Almén, T., Boijsen, E., and Lindell, S. E., 1977. Metrizamide in angiography. I. Femoral angiography. *Acta Radiologica. Diagnosis, 18*, 33–38.

Almén, T., and Trägårdh, B., 1973. Effects of non-ionic contrast media on the blood flow through the femoral artery of the dog. *Acta Radiologica. Supplementum 335*, 197–202.

Amundsen, A. K., Amundsen, P., and Müller, O., 1956. Blood pressure and heart rate during angiocardiography, abdominal aortography, and arteriography of the lower extremities. *Acta Radiologica, 45*, 452–458.

Björk, L., Erikson, U., and Ingelman, B., 1969. Clinical experiences with a new type of contrast medium in peripheral arteriography. *American Journal of Roentgenology, 106*, 418–424.

Boijsen, E., Dahn, I., and Hallböök, T., 1971. Haemodynamic effect of contrast medium in arteriography of legs. *Acta Radiologica. Diagnosis, 11*, 295–309.

Delius, W., and Erikson, U., 1969. Effect of contrast medium on blood flow and blood pressure in lower extremities. *American Journal of Roentgenology, 107*, 869–876.

Efsen, F., and Munkner, T., 1968. Influence of abdominal aortography on arterial blood pressure, cardiac output and heart rate. *Investigative Radiology, 3*, 6–14.

Lindgren, P., Saltzman, G.-F., and Törnell, G., 1968. Vascular reaction to water-soluble contrast media. Significance of concentration and total amount of iodine. *Acta Radiologica. Diagnosis, 7*, 152–160.

Read, R. C., Johnson, J. A., Vick, J. A., and Meyer, M. W., 1960. Vascular effects of hypertonic solutions. *Circulation Research, 8*, 538–548.

Widrich, W. C., Singer, R. J., and Robbins, A. H., 1977. The use of intra-arterial Lidocaine to control pain due to aortofemoral arteriography. *Radiology, 124*, 37–41.

Zinner, G., and Gottlob, R., 1959. Morphologic changes in vessel endothelia caused by contrast media. *Angiology, 10*, 207–213.

Book review

Radiologie. Edited by Heinz Hundeshagen. With contributions by: J. Freyschmidt, G. Hagemann, H. Hundeshagen, K. Jordan, D. Junker, G. Luska, H. Sack, H.-St. Stender, G. Theissen, H. G. Vogelsang, H.-H. Wagner., pp. x+456, illus., 1978 (Springer Verlag, Berlin), DM.58.
ISBN 3-540-08328-6.

It has finally dawned on your reviewer that radiology is a compulsory examination subject for medical students in Germany and that this is the reason why he is reviewing the second book of this type in the space of a few months.

The book successfully manages to pack the basic information a medical student or young doctor would need to know to make the best use of radiation imaging. There are sections on radiation physics, the biological actions of X rays, radiation protection, radiodiagnosis, and nuclear medicine. There is also a short section on radiotherapy. There is good information on the diagnostic techniques available and on the indications for their use. The sections on dose reduction and radiation protection are particularly good. Since the subject matter of this book is not an examination subject in the U.K. it is highly unlikely that the book will find a sale. This is a pity, since any doctor wishing to investigate a patient sensibly and safely needs the information put together in a book such as this. I recommend it.

M. Steiner.

1979, *British Journal of Radiology*, *52*, 173–180

March 1979

Haemophilic arthropathy in the joints of the hands and feet

By Helene Pavlov, M.D., Amy Beth Goldman, M.D., and W. D. Arnold, M.D.

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(*Received May, 1978*)

Abstract

Radiographs of the hands and feet of 72 haemophilic patients were reviewed for peripheral joint involvement. Fifty patients or 69% had changes in the small joints of their hands and/or feet with a total of 160 abnormal joints. In the hands the metacarpo-phalangeal joints were predominantly involved (42 of 50 joints), and in the feet, the metatarso-phalangeal joints (68 of 110 abnormal joints), as well as the posterior subtalar joint (36 of 110 joints). Röntgen abnormalities were characterized by irregularity and/or flattening of the articular cortices.

The involvement of the small peripheral joints in haemophilic patients has not been a primary consideration in previous clinical and radiographic studies because of the more common and more debilitating changes in the large joints. The recognition of involvement of the small joints is described to avoid misinterpretation of the röntgen findings and to appreciate the indicence of involvement, especially with the increased availability of replacement therapy.

Haemophilia is a primary disorder of coagulation complicated by spontaneous intra-articular haemorrhage (Stoker and Murray, 1974). The primary

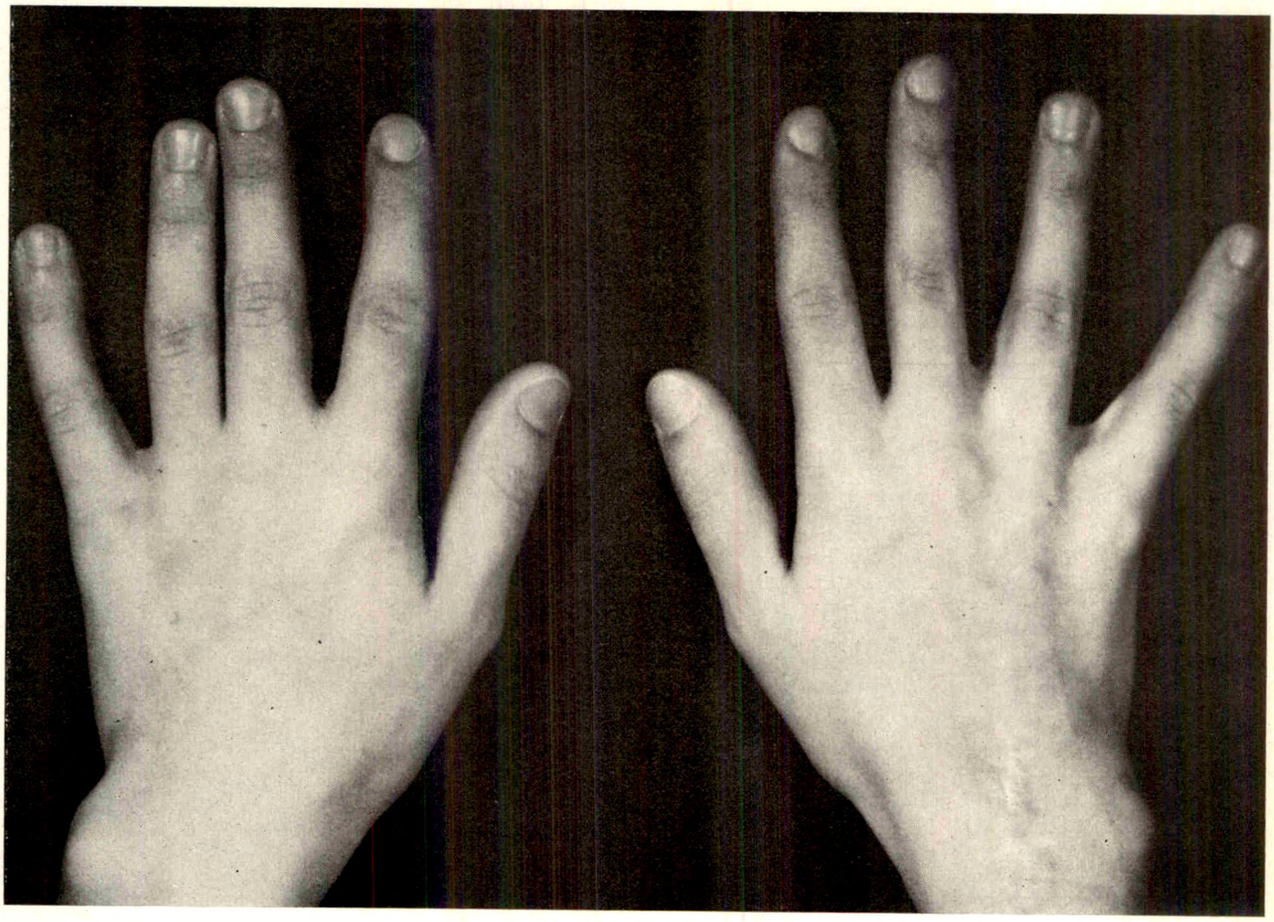

Fig. 1.

Photograph of the dorsum of both hands of a haemophilic patient with deformities of the metacarpal phalangeal joints of the fifth digits, right greater than left.

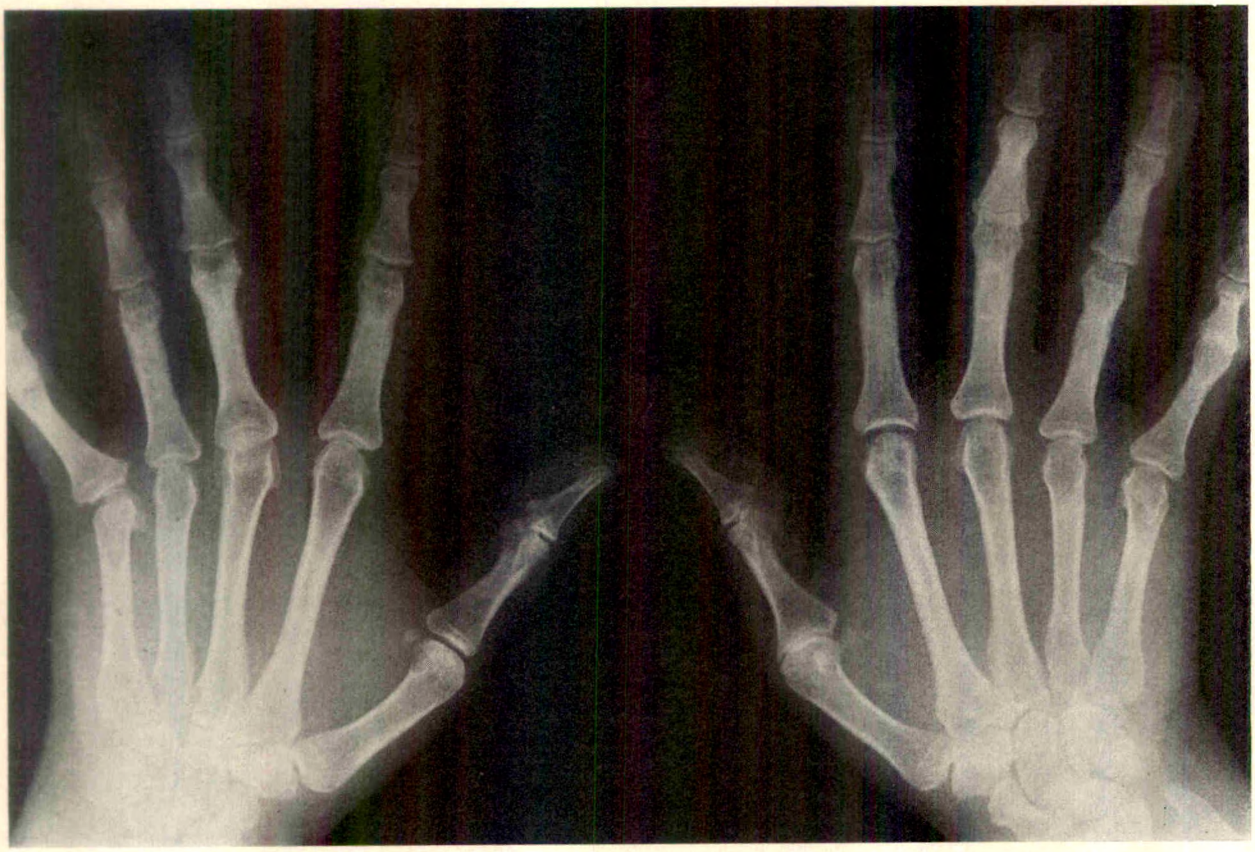

Fig. 2.

On this AP view of both hands, there is flattening and irregularity of the articular cortex of the metacarpal head of the right index finger. Subchondral cysts are present and the joint space is widened in comparison to the other MP joints. The metacarpo-phalangeal joint of the right thumb is narrowed, and the articular surface is slightly flattened. Arthritic changes are also observed in the metacarpal heads of both fifth digits, more marked on the left.

TABLE I

Radiological characteristics in peripheral joints of the hands and feet

	Hands			Feet		
Joints involved	Metacarpal phalangeal	Proximal interphalangeal	Intercarpal	Metatarsal phalangeal	Posterior subtalar	Talonavicular
No. of joints affected	42	5	3	68	36	6
Articular cortices: irregularity and/or flattening	42	5	3	68	36	6
Joint space:						
unchanged	21	0	0	35	0	0
narrowed	19	5	3	14	36	6
Widened	2	0	0	19	0	0
Juxta-articular soft tissue swelling ± haemosiderin deposition	0	1	1	2	36	0
Subchondral cysts	3	0	3	2	1	1
Juxta-articular osteoporosis	0	0	1	0	0	0

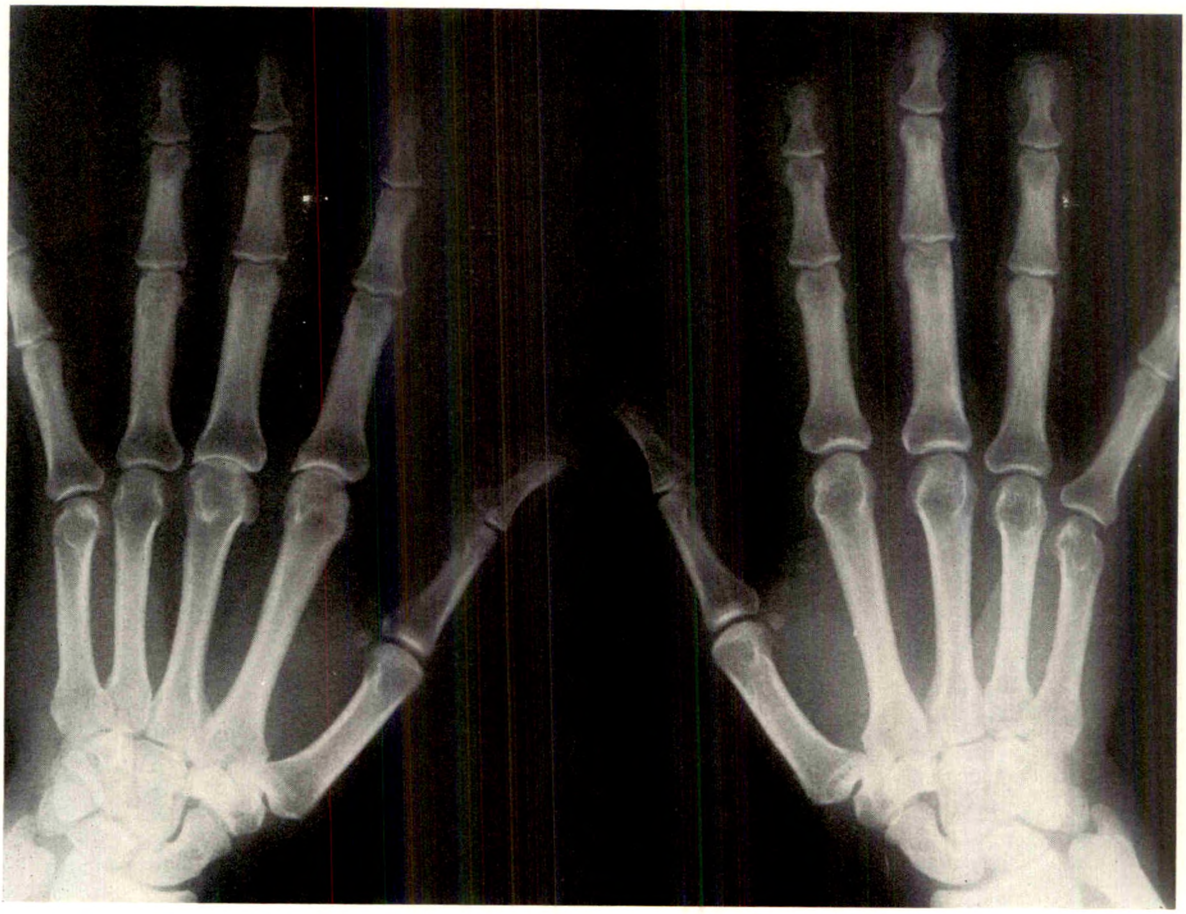

FIG. 3.
An AP view of both hands reveals bilateral and symmetric arthritic changes in the metacarpo-phalangeal joints of the fifth digits. Mild arthritic changes with narrowing and osteophyte formation are also observed at the metacarpo-phalangeal joint of the left index finger.

joints affected are the knees, elbows and ankles (Duthrie *et al.*, 1972; Ghormley and Clegg, 1948).

It is the purpose of this paper to document haemophiliac arthropathy involving the hands and feet, to describe the radiological pattern, and to correlate the clinical significance of the röntgen changes.

MATERIALS AND METHODS

The radiological joint surveys of 72 male patients with haemophilia, followed at The Hospital for

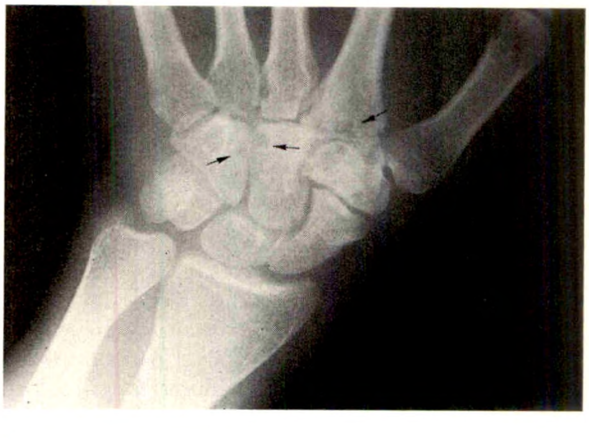

FIG. 4.
An AP view of the left wrist demonstrates intercarpal sclerosis, articular irregularity of the carpometacarpal joints. Subchondral cysts are present (arrows).

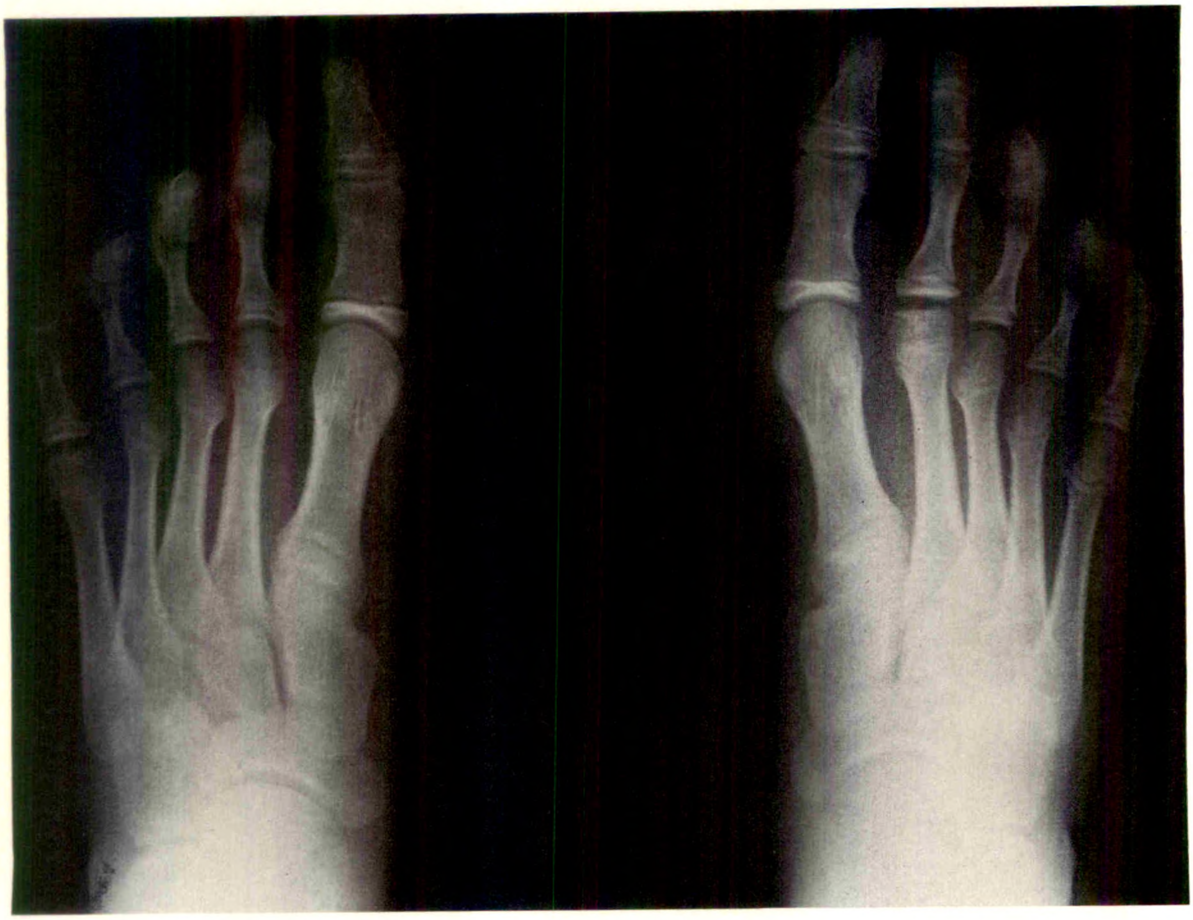

FIG. 5.

An AP view of both feet demonstrates flattening and irregularity of the articular cortices of the metatarsal heads of the right second digit and the left fourth and fifth digits. The joint spaces are slightly widened.

Special Surgery, were reviewed for joint abnormalities in the hands and feet. The patients ranged in age from five to 40 years, with a mean age of 20 years. Sixty-seven patients had factor VIII deficiency (classical haemophilia) and five patients had factor IX deficiency (Christmas disease). The radiographs of the hands and feet were reviewed for: (i) irregularity of the articular cortices, (ii) changes in the width of the cartilage space (narrowing or widening), (iii) juxta-articular soft tissue swelling with or without deposition of haemosiderin, (iv) subchondral cysts, (v) juxta-articular osteoporosis, and (vi) the distribution of the articular abnormalities.

The patients' charts were reviewed for complaints or deformity of the hands and feet. In addition, 20 patients were questioned and five patients were clinically examined regarding pain, swelling, limitation of motion, and bleeds in their hands and feet.

RESULTS

Fifty patients or 69% of the 72 patients with haemophilia had radiological abnormalities in the joints of the hands and feet. A total of 160 joints were abnormal. Eighteen patients had changes in both the hands and the feet, two patients had involvement in their hands alone, and 30 patients had involvement in only their feet.

Arthritic changes involving the hands and wrists were found in 20 patients with a total of 50 abnormal joints with predilection for involvement of the matacarpo-phalangeal joints (42 of 50 joints) (Fig. 1). Radiologically irregularity and/or flattening of the entire articular cortex of the metacarpal head occurred in 42 joints with the joint space relatively unchanged in half the cases (21 joints). In the remainder there was narrowing (19 joints) or widening (two joints) of the cartilage space. Subchondral cysts were present

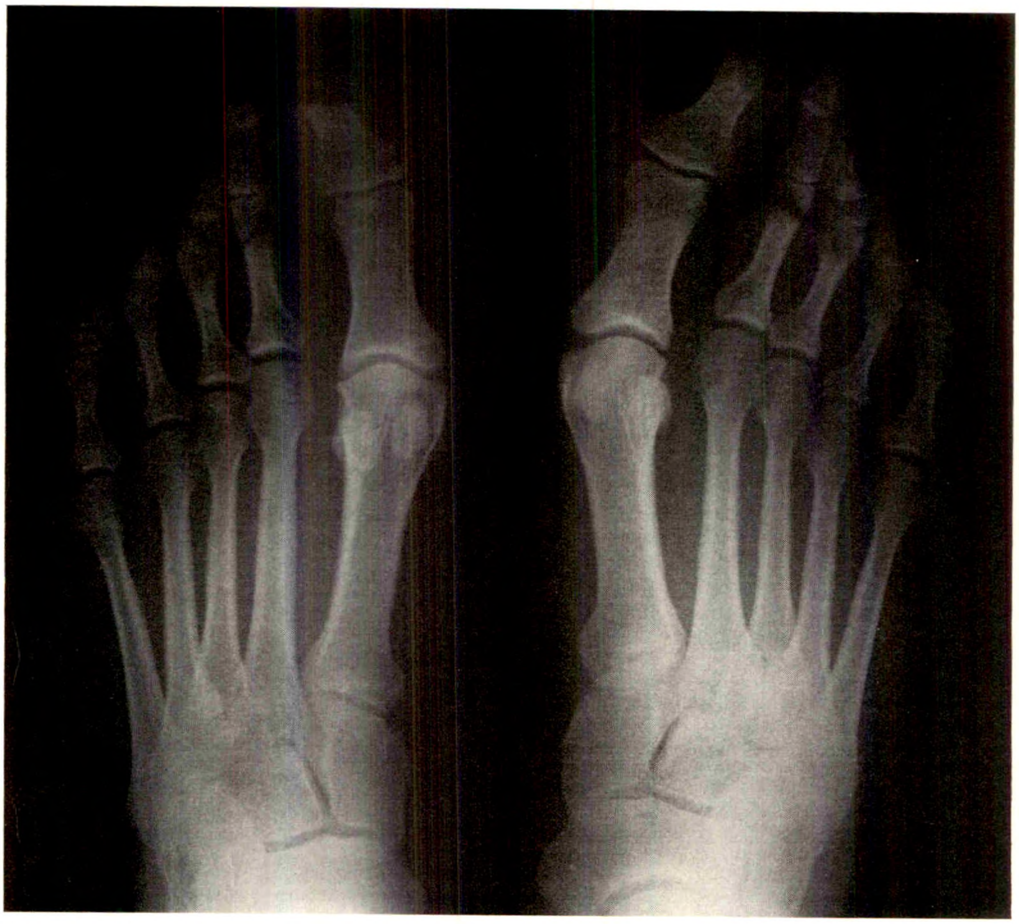

FIG. 6.
An AP view of both feet demonstrates bilateral hallux rigidus deformities, more prominent on the left.

in three joints (Fig. 2). Soft tissue swelling, juxta-articular osteoporosis, and haemosiderin deposits were not observed (Table I). The metacarpo-phalangeal joint of the fifth digit was most frequently involved (Table II), and in five patients the abnormality was bilateral and symmetrical (Fig. 3).

Five proximal interphalangeal joints of the hands of two patients were narrowed and the intercarpal joints of the wrist in three other patients (Table II). The changes in the wrist were accompanied by multiple small subchondral cysts (Fig. 4). Osteoporosis was observed in one involved wrist.

The feet were involved in 48 patients with a total of 110 abnormal joints (Table II). In order of descending frequency, changes were observed in the metatarso-phalangeal joints, the posterior subtalar joints and the talonavicular joints.

There were 68 abnormal metatarso-phalangeal-joints. As in the hands, radiological abnormalities at the metatarso-phalangeal joints were characterized by irregularity and/or flattening of the articular cortex of the metatarsal heads (all 68 joints). The cartilage space was unchanged in width in 35 joints. Widening of the cartilage space was observed in 19 joints, and narrowing of the cartilage space in 14 joints (Fig. 5). Hallux rigidus deformities, with sclerosis and osteophyte formation were observed in 16 cases, none of which had changes in the joint space width (Fig. 6). Increased density in the juxta-articular soft tissues (two joints) and subchondral cysts (two joints) were infrequently observed. One patient had premature epiphyseal ossification of a metatarsal head and subsequent hypertrophy of the epiphysis with cortical irregularity (Figs. 7A and B).

TABLE II

Distribution of peripheral joint involvement in the hands and feet

	No. of joints affected	No. of patients
Hands		
Metacarpal phalangeal joints total number involved 42		
1st digit	3	3
2nd digit	7	4
3rd digit	4	4
4th digit	12	2
5th digit	16	11
Proximal interphalangeal joints		
1st digit	—	—
2nd digit	—	—
3rd digit	2	1
4th digit	1	1
5th digit	2	1
Intercarpal joints	3	3
Feet		
Metatarsal phalangeal joints total number involved 68		
1st digit	18	11
2nd digit	10	7
3rd digit	12	12
4th digit	17	15
5th digit	11	9
Posterior subtalar joints	36	25
Talonavicular joints	6	5

TABLE III

Analysis of posterior subtalar joint involvement

36 joints affected	25 patients involved
Isolated changes without joint involvement in hands and feet	8
Associated with joint involvement in the feet	8
Associated with joint involvement in the hands	6
Associated with joint involvement in the hands and feet	3
Association of haemophilic arthritic changes in the ankle joint	
Definitive	30
Equivocal	5
Negative	1

There was no evidence of juxta-articular osteoporosis or periosteal new bone formation (Table I). The first digit (18 joints) the fourth (17 joints) and the fifth (11 joints) digits were most frequently involved. Bilateral and symmetrical changes in the metatarsals were present in only five cases (Table II).

There were 36 abnormal posterior subtalar joints. In 11 instances, the changes were bilateral. Articular abnormalities including narrowing, subchondral cysts, sclerosis and irregularity of the articular cortices were observed (Figs. 8A, B, C). In 30 of the 36 cases there were severe arthritic changes in the ipsilateral ankle, in five cases the ankle was only minimally abnormal, and in one case the ankle was entirely normal (Table III).

Involvement of the talonavicular joints, characterized by narrowing and subchondral sclerosis was present in five patients and was bilateral in one.

Of the 25 patients clinically questioned, 18 had a history of recurrent bleeds into their hands and feet requiring treatment. Only one patient had clinical deformity corresponding with X-ray changes, i.e. a 20% flexion contracture of the 2nd metacarpophalangeal joint of the hand. Three of the seven patients without a history of bleeding episodes in their hands or feet had X-ray changes in these areas. Several other patients had finger and toe deformities clinically, but normal radiographs. The latter findings concur with recent reports (Arnold and Hilgartner, 1977) that bleeds in the hands usually resolve without residual clinical changes. However, according to the incidence of radiological deformities in the hands and feet, significant bleeding episodes in these areas are evidently more common than previously recognized.

Discussion

Arthritic changes in the knees, ankles and elbows are earliest and best recognized sequelae of spontaneous intra-articular haemorrhages of haemophilia. However, intra-articular bleeds and arthritic changes also occur in the small joints and in our series, radiological abnormalities in the small peripheral joints of the upper and lower extremities occurred in 69% of 72 haemophilic patients. As in the large joints, the lower extremity was more frequently involved (110 of 160 joints) than the upper extremity (50 of 160 joints). In both the hands and feet, the MP joints were most frequently involved. As in the knee or elbow, X-ray findings included irregularity and/or flattening of the articular cortices as well as premature epiphyseal ossification and overgrowth. Unlike large joint haemophilic arthropathy, haemosiderin deposition in the soft tissues (two of 110 MP joints) and subchondral cysts (five of 110 MP joints) were infrequently observed. The width of the cartilage space varied and the distribution of the

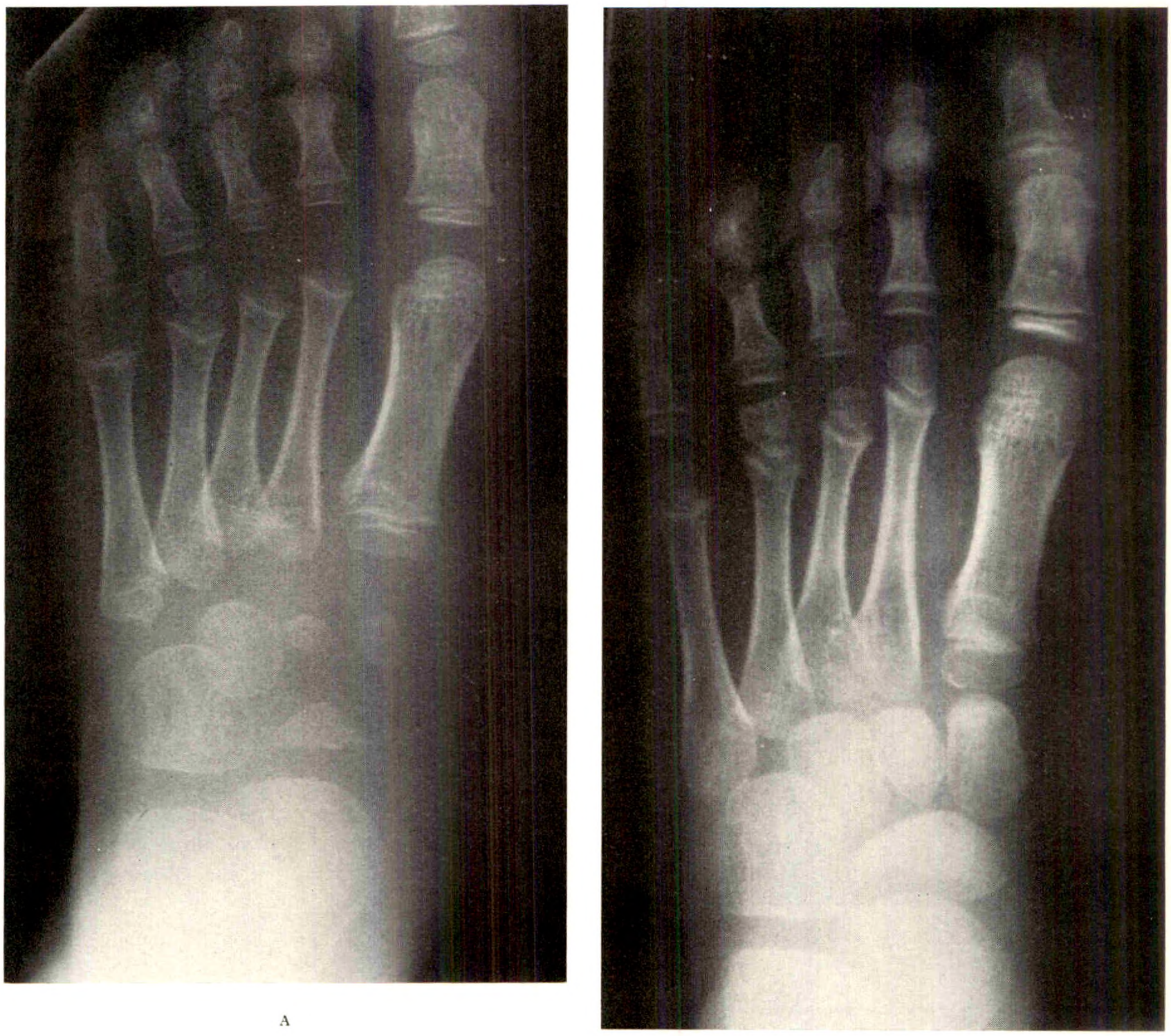

FIG. 7.

(A) An AP view of the left foot demonstrates premature ossification of the fourth metatarsal epiphyses.

(B) A follow-up film of the left foot reveals irregularity and flattening of the articular cortex of the fourth metatarsal head as well as overgrowth.

changes in the MP joints was usually asymmetric. The posterior subtalar joint was the second commonest site of articular abnormalities (36 of 160 joints). Less frequent sites included the talonavicular joint (six joints), the proximal interphalangeal joints (five joints) and the intercarpal joints (three joints).

The pathophysiology of articular abnormalities in the small peripheral joints is probably the same as that in the large joints and a result of recurrent intra-articular haemorrhage. The amount of bleeding necessary to produce changes in the small joints is minimal compared to that of the large joints. The pain and disability of a large intra-articular joint haemorrhage most probably diverts attention away from less significant traumatic events and may account for the lack of complaints referable to the hands and feet despite the high incidence of radiological and clinical abnormalities.

The distribution of the large joints involved in haemophilia can be related to several factors. First, due to their peripheral location, the knees, elbows, and ankles are more susceptible to repetitive trauma than the centrally located articulations such as the

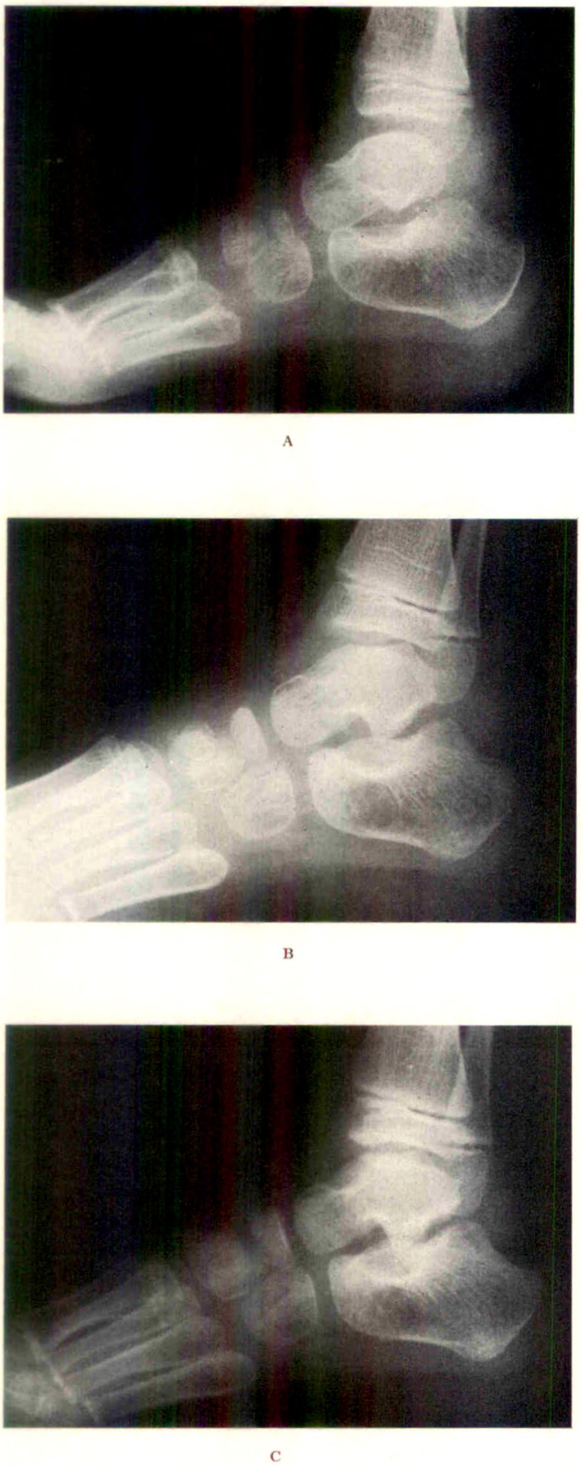

FIG. 8.

(A) A lateral view of the right ankle (11.12.72) reveals juxta-articular haemosiderin deposits. The articular surfaces are smooth.
(B) Follow-up lateral view of the right ankle (2.12.74) reveals irregularity of the superior surface of the talus and the posterior subtalar joint is sclerotic and irregular.
(C) Follow-up lateral view of the right ankle (6.9.75) reveals further progressive arthritic changes.

hips and shoulders. Second, mechanical stress is considered more critical to joint vulnerability than weight-bearing and third, hinge-type articulations stabilized by muscles and tendinous structures are at higher risk than ball-and-socket joints stabilized by osseous architecture (De Palma, 1967; Stoker and Murray, 1974). These principles can easily be applied to the MP joints which are peripheral, hinge-type articulations, stabilized only by the surrounding soft tissues.

The recent increase in availability of factor VIII has changed the therapeutic approach to spontaneous intra-articular haemorrhage. In a recent clinical study (Lancourt *et al.*, 1977) of 200 patients with haemophilia, ten cases presented with wrist and digital haemarthrosis, and nine were of sufficient severity to merit immediate replacement therapy.

Recognition of the radiological articular abnormalities in the hands and feet of haemophilic patients is important to exclude other aetiologies for these deformities such as trauma, infarct or infection. In addition, identification of the early radiological and clinical signs may indicate the need for early treatment with factor VIII.

REFERENCES

ARNOLD, W. D., and HILGARTNER, M. W., 1977. Hemophiliac arthropathy; current concepts of pathogenisis and management. *Journal of Bone and Joint Surgery, 59A*, 287–305.

DE PALMA, A. F., 1967. Hemophilic arthropathy. *Clinical Orthopaedics and Related Research, 52*, 145–165.

DUTHRIE, R. B., MZTTHEWS, J. M., RIZZA, C. R., and STEEL, W. M., 1972. *The Management of Musculo-Skeletal Problems in the Haemophiliacs.* Blackwell Scientific, Oxford.

GHORMLEY, P. K., and CLEGG, R. S., 1948. Bone and joint changes in haemophilia: with report of so-called haemophilic pseudotumors. *Journal of Joint and Bone Surgery, 30A*, 589–600.

LANCOURT, J. E., GILBERT, M. S., and POSNER, M. A., 1977. Management of bleeding and associated complications of haemophilia in the hand and forearm. *Journal of Bone and Joint Surgery, 59A*, 451–460.

STOKER, D. J., and MURRAY, R. O., 1974. Skeletal changes in hemophilia and other bleeding disorders. *Seminars in Roengenology, 9*, 185–193.

1979, *British Journal of Radiology*, *52*, 181–183 MARCH 1979

Intrathoracic rib: radiographic features of two cases

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ABSTRACT

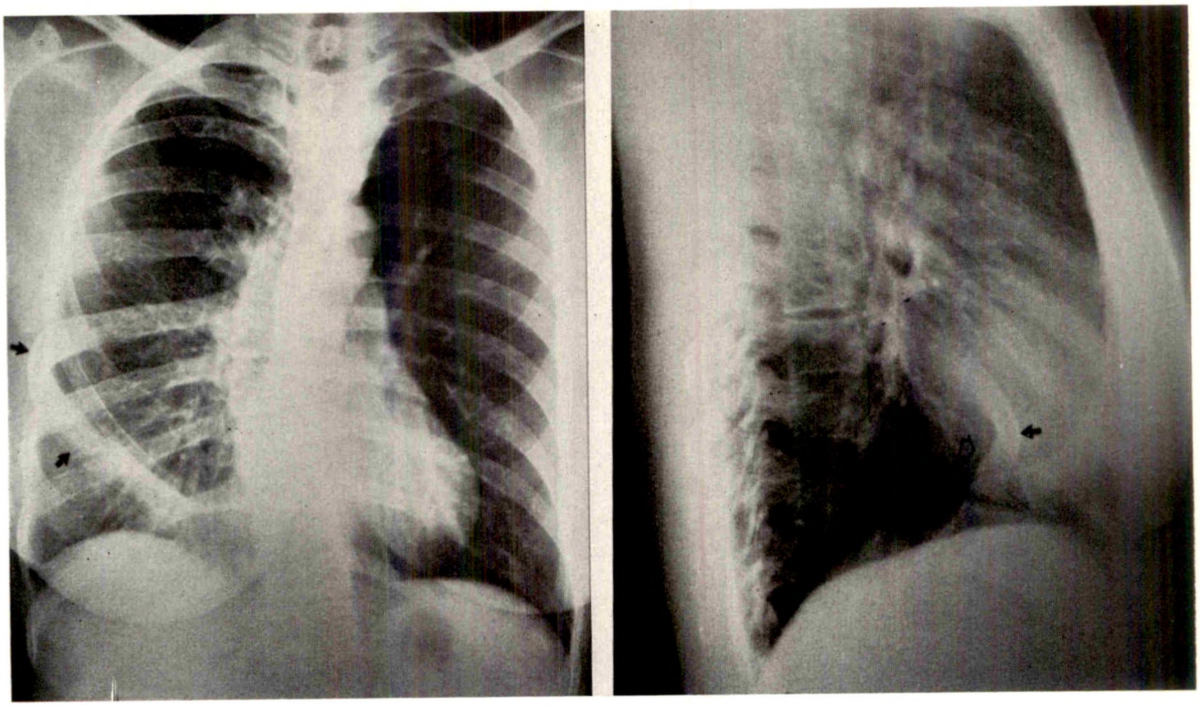
Two cases of intrathoracic rib are presented. In one of these the anomalous rib was not supernumerary, and the investing layers of pleura caused the rib to appear abnormally dense. The relevant literature is briefly reviewed.

Minor anomalies of the bony thoracic cage are not uncommon, being found in approximately 1% of the normal population (White, 1929; Etter, 1944; Weinstein and Mueller, 1965; Freed, 1972). Intrathoracic ribs are usually supernumerary and are exceptionally rare (Fraser and Paré, 1977). Although they are commonly asymptomatic and often an incidental finding (Weinstein and Mueller, 1965), their importance to the radiologist lies in the fact that they may simulate intrathoracic pathology and lead to an unnecessary thoracotomy (Plum *et al.*, 1957; Von Ronnen and Jongh, 1962). Fifteen cases have been documented in the literature since the anomaly was first described by Lutz in 1947. Two recently encountered cases are the basis for this report. In one case, the anomalous rib was supernumerary and descended vertically through the left upper lobe posteriorly. In the other case, the intrathoracic rib was not supernumerary and began its anomalous course in the right mid-axillary line. Because this rib was surrounded by invaginated visceral and parietal pleura, it appeared abnormally dense on postero-anterior projection. Displacement of the oblique fissure by this rib was evident.

CASE REPORT

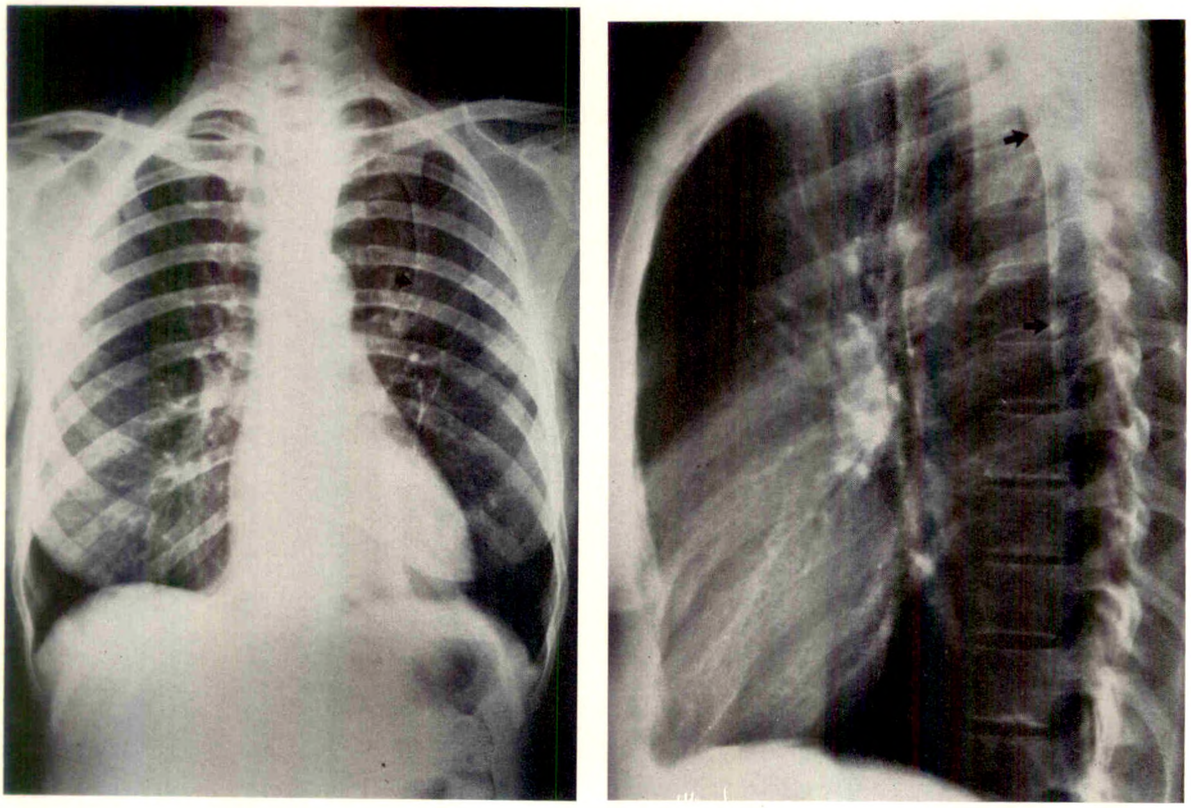
Case 1.

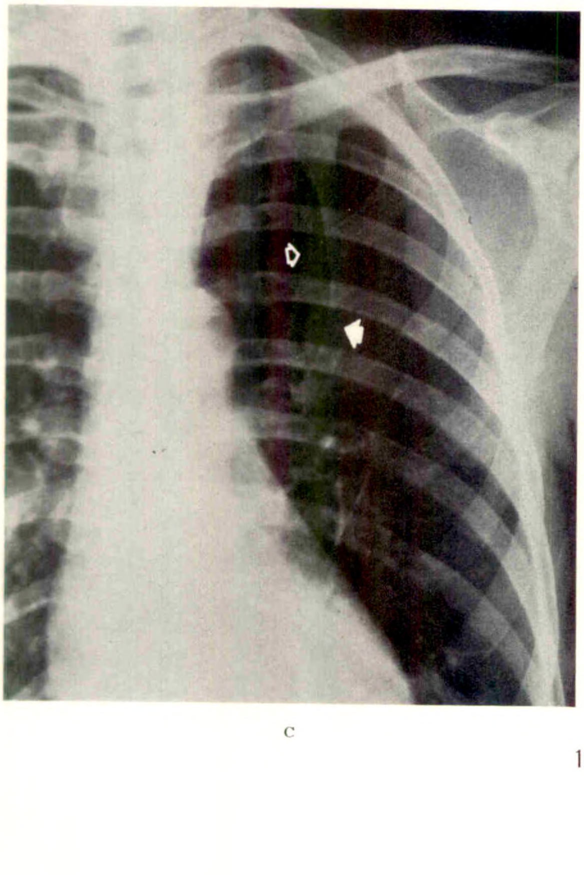
The patient, a 44-year-old black female, was found to have a thoracic deformity on a routine chest radiograph. She was completely asymptomatic. There were no significant illnesses in the past history, and she was the product of a normal pregnancy. Physical examination revealed no abnormality. A chest radiograph (Fig. 1A and B) showed an intrathoracic extension of the right 7th rib, the anomalous portion entering the thorax in the mid-axillary line. The rib



A FIG. 1. *Case 1.* B

There is increased density of the anterior portion of the right 7th rib (closed arrows), which is shown to be intrathoracic on the lateral view. There is hypoplasia of the adjacent rib and a mid-thoracic scoliosis. The oblique fissure is displaced (open arrows).





appeared abnormally dense on the PA projection because of the investing four layers of pleura. There was hypoplasia of the anterior portion of the right 6th rib and a moderate mid-thoracic scoliosis. Pulmonary function studies revealed a normal forced vital capacity and FEV_1 with FEV_1/FVC ratio of 79.3. In view of the lack both of symptoms and objective evidence of a restrictive pulmonary defect, no treatment was advised.

Case 2.

A 48-year-old white female was referred to the University of Chicago Hospitals and Clinics for investigation of hypertension and proteinuria. A chest radiograph revealed a supernumerary intrathoracic rib on the left side. The anomalous rib arose from the posterior portion of the left 3rd rib and descended posteriorly into the chest (Fig. 2A and B). A faint parallel density accompanied the anomalous rib (Fig. 2C) and was attributed to the invaginated layers of pleura. The patient had no symptoms referable to the thoracic cage abnormality and surgical interference was not advised.

Discussion

Congenital anomalies of the ribs are common and include cervical rib, bifid anterior rib, and fusion of

Fig. 2. *Case 2.*

A vertically oriented supernumerary rib is demonstrated (closed arrows) with its investing layers of pleura (open arrows).

adjacent ribs (Steiner, 1943). Supernumerary intrathoracic (Freed, 1972) and transthoric ribs (Shoope, 1969) have been previously described. Review of the literature reveals that, including the two cases described here, these are more common on the right side in the ratio of 12:5 and there is no significant sexual predominance. An intrathoracic rib is usually an incidental finding. In every reported case, the anomaly has been unilateral and not associated with other skeletal deformities. One case has been reported with an associated right-sided aortic arch (Whitlark and Engels, 1962). The anomalous rib usually arises either from the postero-inferior margin of another rib (as in case 2) or directly from a vertebral body. It may have a fibrous, diaphragmatic attachment, which can cause a restrictive ventilatory defect. In case 2, the intrathoracic rib arose from the inferior border of the left 3rd rib posteriorly, and an adjacent shadow representing enveloping pleura was seen. This appearance is unlikely to cause diagnostic confusion. However, when the anomalous rib arises directly from a vertebral body, it may descend in the paravertebral space and be mistaken for persistent right lower lobe collapse (Stevenson and Merendino, 1956), a mediastinal mass or cyst, anomalous vessel (Plum *et al.*, 1957), or a paravertebral mass (Von Ronnen and Jongh, 1962). In the past, some of these patients have been subjected to unnecessary thoracotomy.

To our knowledge, the anomaly demonstrated in case 1 has not been previously reported. The anomalous rib was not supernumerary, and the abnormal course of the rib was not apparent on the frontal projection. The anterior portion of the rib appeared sclerotic due to the superimposed density of the invaginated pleural layers, and an initial impression of fibrous dysplasia or Paget's disease was given. There was, however, a thoracic scoliosis and hypoplasia of the anterior portion of the rib immediately superior to the anomalous rib. The lateral projection demonstrated that the rib negotiated an abnormal course into the thorax and caused anterior displacement of the greater fissure.

While the abnormality can usually be diagnosed with confidence on the conventional chest radiograph, on occasion, supplementary radiological investigations, such as fluoroscopy and tomography, may be necessary.

Intrathoracic ribs are rare and may be mistaken for significant intrathoracic pathology. An awareness of the anomaly and its differing radiological appearances, however, should prevent unnecessary investigations and surgery.

REFERENCES

Etter, L. E., 1944. Osseous abnormalities of the thoracic cage seen in forty thousand consecutive chest photoroentgenograms. *American Journal of Roentgenology, 51*, 359–363.

Fraser, R. G., and Paré, J. A. P., 1977. In *Diseases of the Chest*, 2nd ed., vol. 1, p. 165 (W. B. Saunders Co., Philadelphia).

Freed, C., 1972. Intrathoracic rib: a case report. *South African Medical Journal, 46*, 1165–1167.

Lutz, P., 1947. Ueber eine ungewöhnliche Rippenanomalie, zugleich ein Beitrag zur distalen Rippengabelung. *Weiner Klinische Wochenscrift, 59*, 846–849.

Plum, G. E., Hayles, A. B., Bruwer, A. J., and Clagett, O. T., 1957. Supernumerary intrathoracic rib: case report. *Journal of Thoracic and Cardiovascular Surgery, 34*, 800–803.

Shoope, J. D., 1969. Transthoracic rib. *Radiology, 93*, 1335–1336.

Steiner, H. A., 1943. Roentgeologic manifestations and clinical symptoms of rib abnormalities. *Radiology, 40*, 175–178.

Stevenson, J. K., and Merendino, K. A., 1956. Two unusual congenital anomalies of thorax: (1) supernumerary ribs and (2) abnormal intrathoracic rib: case report. *Journal of Thoracic and Cardiovascular Surgery, 32*, 521–527.

Von Ronnen, J., and Jongh, R., 1962. Description de deux cas de côte de intrathoracique. *Annales de Radiologie, 5*, 639–647.

Weinstein, A. S., and Mueller, C. F., 1965. Intrathoracic rib. *American Journal of Roentgenology, 94*, 587–590.

White, J. D., 1929. Abnormalities of bony thorax. *British Journal of Radiology, 2*, 351–355.

Whitlark, F. L., and Engles, E. P., 1962. Supernumerary left intrathoracic rib with right-sided aortic arch. *Journal of the American Medical Association, 179*, 968.

Book review

Gray-scale Ultrasound: a Manual for Physicians and Technical personnel. By R. J. Bartrum and H. C. Crow, 1977, pp. xiii+216, illus., (W. B. Saunders Co. Sussex), $10.00.

This is one of many books of ultrasound recently released onto the market. Like others it gives the impression of being written quickly. Its cover describes the book as "A Manual for Physicians and Technical Personnel" and it has a number of useful practical points for those setting up a department with no previous experience. The text is often juvenile and too frequently interrupted with Americanisms which are very irritating.

Unfortunately many of the scans illustrated are technically poor and one wonders why half the space is used up on physics and technique.

The clinical chapters are better but I am surprised that no mention is made of ultrasound scanning of the eye.

A. B. Ayers.

1979, *British Journal of Radiology*, *52*, 184–188

Ultrasound in the detection of chronic liver disease (the "bright liver")

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ABSTRACT

The association of high amplitude echoes returned from the liver and advanced cirrhosis is well recognized. We have become increasingly aware of a bright liver echo pattern in relatively mild cases of cirrhosis and in other chronic liver diseases. The pattern is very characteristic but non-specific in pathological terms. We have undertaken a small pilot study based on the observation of this characteristic ultrasound appearance to assess its clinical significance. Recognition of this pattern has always corresponded with liver disease of one of five types: cirrhosis, fatty infiltration, portal tract fibrosis, severe hepatitis or longstanding congestive cardiac failure. Although the use of ultrasound appears to be sensitive in the detection of generalized liver disease, it is relatively non-specific.

It has been recognized for some years that in established cirrhosis high amplitude echoes may be returned from the liver. Many authors stress that this occurs in advanced disease only (Carlsen, 1975) (Sanders and Sanders, 1977). Fatty infiltration of the liver also may give rise to high amplitude echoes, evenly distributed throughout the liver parenchyma. It is suggested that fatty infiltration and cirrhosis may be distinguished from each other by the coarseness of the echo pattern and the marked distal attenuation that occurs in the latter (Taylor *et al.*, 1976).

The pathology of cirrhosis is the progressive disruption of the liver architecture with replacement by fibrous tissue. Although not firmly established, it is thought that the echoes from an organ predominantly arise from the fibrous skeleton (Fields and Dunn, 1973). Although this is probably an over simplification, our own studies with post mortem ultrasound and histological correlation show that with necrosis and destruction of liver tissue the region becomes relatively non-reflective, this being true of both abscesses and metastases. We have also observed that the non-reflective halo in the "target metastases" represent regions of sinusoidal ectasia. Much narrower non-reflective rings demarcating metastases also have the same aetiology (Dewbury and Joseph, 1978). Cirrhotic livers with increased fibrous tissue content may be expected to generate increased echoes of higher amplitude. Quantitative A scan analysis has shown this to be true (Mountford and Wells, 1972).

Over the past two years we have become increasingly aware of a characteristic echo pattern seen on the B scan in some liver diseases. The basic pattern consists of closely packed high amplitude echoes throughout the liver. A further feature is the posterior attenuation of the beam in some instances. Often the tram line pattern of the portal veins is lost and it is difficult to distinguish between the portal veins and hepatic veins, particularly in the periphery. Stretching of vessels is a further finding in some of the livers with this type of echo pattern. These findings are observed with the usual TGC settings (2db/cm). It may require increase of the TGC and increased gain settings to obtain optimal views of the posterior aspects of the livers in those showing increased attenuation. This tightly packed, increased echo pattern has been observed by us in cirrhosis, portal fibrosis, chronic active hepatitis, fatty change and severe or longstanding congestive cardiac failure. This liver pattern we have called the "bright liver". This study has been undertaken to assess the significance of the "bright liver". We are unaware of any other such studies reported in the English literature.

SUBJECTS AND METHODS

The examinations reported here were all carried out on a commercially available grey-scale machine using a long internally focussed 2.25 MHz probe. The assessment of the liver parenchyma was made on longitudinal scans of the liver obtained by the standard single sweep technique, in suspended inspiration. The transverse sector scans were not used for the assessment of the bright liver pattern. The characteristic "bright liver" echo pattern was detected at standard instrument settings (mentioned above) although slightly higher gain settings were often required for optimal results.

Over a ten-month period a consecutive series of 60 patients were seen with a "bright liver" pattern on the ultrasound images. In no case was the histo-

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Requests for reprints to K. C. Dewbury.

TABLE I

"BRIGHT LIVER PATTERN"

Histological findings	"Bright liver"	Isotope positive (cirrhotic pattern)	Notable posterior attenuation	Clinically unsuspected
1. Cirrhosis	27	16/20+80%	16/27	2
2. Portal fibrosis and fatty infiltration	16	5/11+45%	8/16	3
3. Severe hepatitis	2	0/2+0%*	0	0
4. Cardiac cirrhosis	2	—	0	0

Note: There were no false positives.

*Although the two patients in this series did not yield a "cirrhotic" pattern on the isotope images, it is well known that this is one of the causes of the cirrhotic pattern with increased splenic and marrow uptake.

logical diagnosis known at the time of examination, and follow-up was by analysis of the patients' records. A subsequent biopsy report was available on 45 of the patients. ^{99}Tc^{m} sulphur colloid images were available in 35 patients.

RESULTS

The findings in the 45 patients on whom histology is available are presented in Table I. There are three main histological groups. Cardiac cirrhosis is included as a fourth group. Biopsies were not done on either of these patients, however the clinical picture in both instances was of severe congestive cardiac failure, so they have been included. The criteria for the diagnosis of a cirrhotic pattern on the isotope images are transfer of activity to the spleen and bones and splenic enlargement. The liver size is variable depending on the clinical stage of the disease. An attempt has been made to subjectively assess the incidence and significance of notable posterior attenuation by review of the ultrasound images and results are recorded in Table I. In the 27 cases of cirrhosis some showed micronodular change, some macronodular and others showed a mixed pattern. In addition 30% of this group showed fatty infiltration. The severity of change reported was variable ranging from mild to severe. Review of the ultrasound images showed no correlation with the type, or severity of the pathological change recorded. A typical example of the bright echo pattern seen in cirrhosis is illustrated in Fig. 1A. There is marked distal attenuation of the beam. The A scan from this patient is shown in Fig. 1B. The parenchymal echoes are half to three-quarters the size of the diaphragmatic echo. Figs. 2A and B are corresponding scans from a normal patient for comparison. Marked distal attenuation did not always occur in cirrhosis. An example of this appearance is seen in Fig. 3. The liver

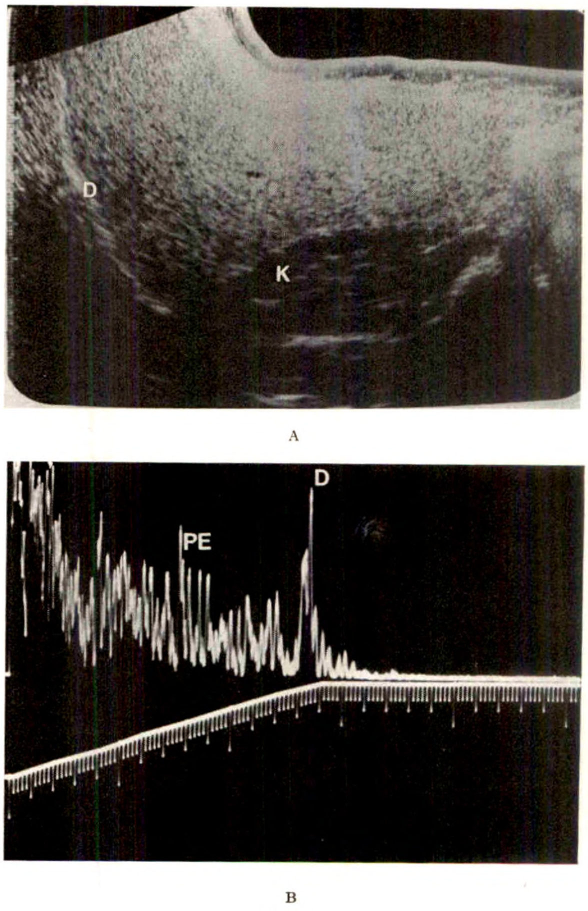


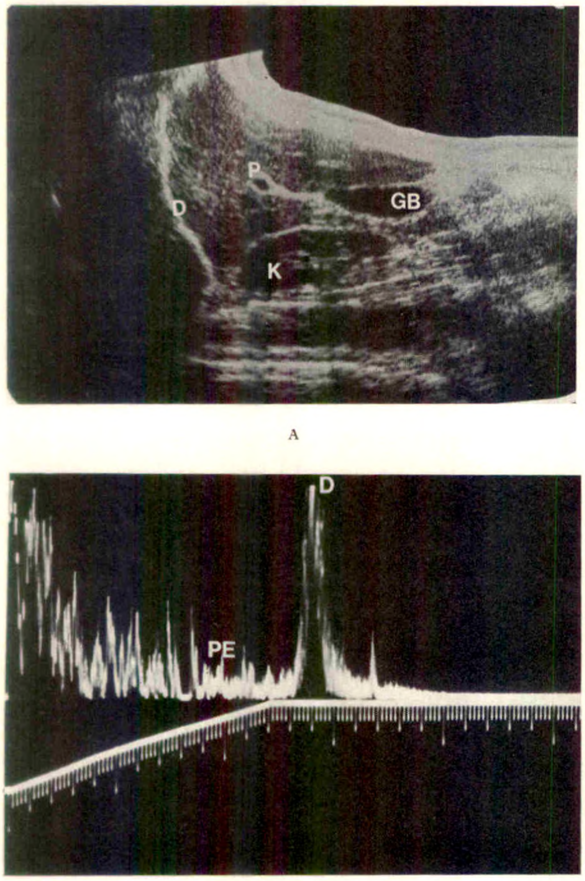
FIG. 1

(A) Cirrhosis. Note the typical bright echo pattern. The portal vein walls can no longer be seen. The liver is enlarged and there is distal attenuation of the beam. D – Diaphragm. K – Kidney.

(B) A scan from the same patient. Note the parenchymal echoes (PE) are half to three-quarters the size of the diaphragmatic echo (D).

is enlarged and bright. The portal vein walls are lost. There is a trace of acitic fluid under the liver. Isotope studies were available in 20 patients in this group and suggested cirrhosis in 16.

In the second group, eight patients showed mixed changes of portal tract fibrosis and fatty infiltration. Seven patients showed varying degrees of fatty infiltration alone and one patient showed only extensive portal tract fibrosis. Once again in this group it was not possible to correlate the ultrasound images with the specific pathology or the severity of pathological change. Figure 4 is a scan of a patient with mixed fatty infiltration and portal tract fibrosis. A number of calculi is present in the gall-bladder. Isotope studies were available in 11 patients and showed changes consistent with cirrhosis in five instances. The final small group of two patients with severe changes of hepatitis B, one with bridging necrosis. Fig. 5 is a scan from this patient. The isotope studies were normal in both instances. In the remaining 15 patients on whom biopsies have not been done, or are not available, two patients were in severe congestive cardiac failure and are included in Table I, and five patients have strong clinical evidence of chronic liver disease (but are not included).



A

B

FIG. 2

(A) Normal liver for comparison with Fig. 1 (A). P – Portal vein. D – Diaphragm. GB – Gall Bladder. K – Kidney.

(B) A scan from the same patient for comparison with Fig. 1 (B). Note the parenchymal echoes (PE) are under half the size of the diaphragmatic echo (D).

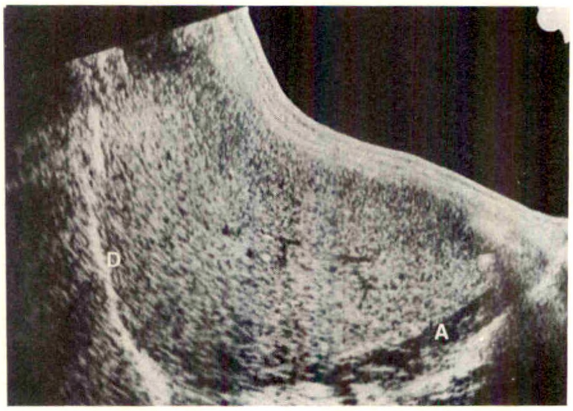


FIG. 3.

Cirrhosis. Note the typical bright echo pattern with loss of visualization of the portal vein walls. In this patient there is no significant distal attenuation of the beam at normal TGC settings. There is a trace of ascites (A). D – Diaphragm.

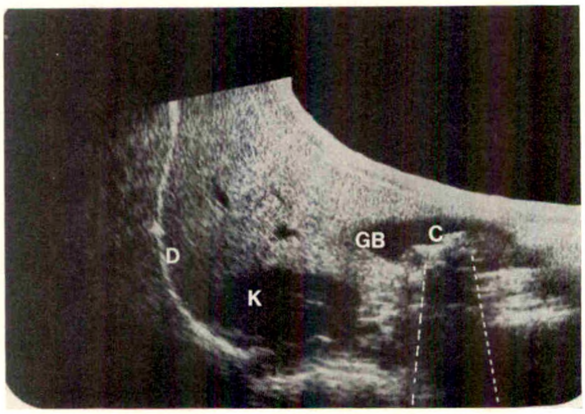


FIG. 4.

Fatty infiltration and portal tract fibrosis. Note the typical bright echo pattern of the liver parenchyma. There is no significant distal attenuation. There are multiple calculi (C) in the gall-bladder (GB). D – Diaphragm. K – Kidney.

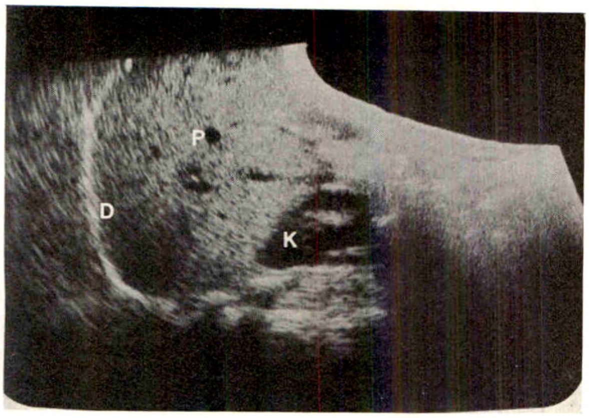


FIG. 5.

Hepatitis B. The liver shows a bright echo pattern. The portal vessels (P) can be seen but there is loss of the normal bright cuff around them. D – Diaphragm. K – Kidney.

Notable distal attenuation of the sound beam occurs in approximately half of the patients and does not appear to correlate closely with the type and severity of pathological change. Comparison of Figs. 3, 4 and 5 shows how similar the appearances are in three cases with different pathological diagnoses. In none of these instances is notable distal attenuation present. This observation, however, remains a subjective assessment and a more objective measurement would be of great value. This observation of course also applies to the recognition of the "bright liver" pattern. However, it is of some importance that there have been no false positive diagnoses by ultrasound in this series. The presence of a "bright liver" pattern has always correlated with proven liver disease. In five cases significant liver disease was first suggested by the ultrasound images, when there was no strong clinical suspicion. The scans were performed due to mildly abnormal liver function tests.

During the course of this study we have encountered five cases of established cirrhosis in whom the ultrasound images appear normal. Interestingly in all these cases isotope studies showed a cirrhotic pattern.

DISCUSSION

The recognition of the "bright liver" echo pattern has considerable diagnostic value. Although previous investigators have commented upon the occurrence of high amplitude echoes in both fatty infiltration and cirrhosis, stress has been upon finding this in advanced disease. In these circumstances the diagnostic value of this appearance would be limited, this has not been our experience. We have had no false positive examinations to date, although the finding of this echo pattern alone is relatively non-specific in pathological terms. It is of some relevance, however, that portal tract fibrosis, fatty infiltration and cirrhosis are frequently part of the same pathological spectrum. Correlation with the severity of pathological change is poor. Both very early cirrhosis and minor fatty change have been detected, whilst established cirrhosis has appeared normal. This fact is perhaps rather surprising and we have no explanation for it. The more relevant observation is that early abnormality may be detected, and that in 13% of our series the ultrasound images were the first indication of significant liver disease.

It is clear that ultrasound imaging will not exclude cirrhosis. The reliability of ultrasound in the detection of cirrhosis is not known. A prospective study is now under way to assess this.

In established cirrhosis we have found isotope imaging to be accurate, but at the other end of the spectrum where only portal fibrosis and fatty infiltration is present the accuracy in this series is 45%.

No mention has yet been made of ascites and portal vein enlargement in portal hypertension or of hepatic vein enlargement in congestive cardiac failure. We have found these useful diagnostic observations present in some of our cases. However, there tend to be changes occurring in long established and severe disease which limits their real diagnostic value.

CONCLUSION

A characteristic "bright liver" echo pattern is described on the basis of a subjective assessment of ultrasound images. This is recognized at standard machine settings. The clinical relevance of this has been assessed in a consecutive series of unselected patients, on whom biopsy reports subsequently became available. Recognition of this liver echo pattern has always corresponded with proven liver disease of one of five types: cirrhosis, fatty infiltration, portal tract fibrosis, severe hepatitis, or longstanding cardiac failure. Although the use of ultrasound appears to be sensitive in the detection of generalized liver pathology, it is relatively non-specific. The use of both ultrasound and sulphur colloid liver imaging would increase the detection of chronic liver disease.

REFERENCES

CARLSEN, E. N., 1975. Liver, gall bladder and spleen. *Radiological Clinics of North America*, 13, 543–556.

DEWBURY, K. C. and JOSEPH, A. E. A., 1978 (Unpublished data.)

FIELDS, S. and DUNN, F., 1973. Correlation of echographic visualizability of tissue with biological composition and physiological state. Letter to editor. *Journal of Accoustical Society of America*, *54*, 809–812.

Mountford, R. A. and Wells, P. T. N., 1972. Ultrasonic liver scanning: the A scan in the normal and in cirrhosis. *Physics in Medicine and Biology*, *17*, 261–269.

Sanders, A. D. and Sanders, R. C., 1977. The complementary use of B Scan ultrasound and radionuclide imaging techniques. *Journal of Nuclear Medicine*, *18*, 205–220.

Taylor, K. J. W., Carpenter, D. A., Hill, C. R., and McReady, V. R., 1976. Greyscale ultrasound imaging. *Radiology*, *119*, 415–423.

Book review

Principles of Surgical Oncology. Edited by Ronald W. Raven, pp. 519, 1977, (Bailliere Tindall, London), £28·00. ISBN 0-7020-0670-X.

Oncology is a wide subject which encompasses the many facets of causation, prevention, diagnosis and treatment of tumours. No one can be an expert in all its aspects. Advances in knowledge are therefore more likely to follow mutual understanding and close co-operation of specialists in the different clinical and laboratory disciplines.

Most surgeons have a relatively limited knowledge of oncology due to the fact that, whether they be general or specialist surgeons, only part of their practice is devoted to the management of tumours. There is, therefore, a need for a book written specifically for surgeons so that they can fulfill their role in a multidisciplinary team. This book aims to meet this need by giving an overall picture of the subject and its fundamental principles. It makes no attempt to define the place of surgery in the management of individual tumours.

The book contains a great deal of information on basic subjects such as tumour biology and biochemistry and the relationship between tumours and the endocrine and immune systems. Carcinogenesis and world-wide epidemiology are particularly well covered. The editor was, however, probably over-zealous in including a chapter devoted to a mathematical model of the dividing cell and to allow fourteen pages of references on endocrinology.

Diagnosis and treatment are of more immediate interest to the surgeon. The chapter on pathological diagnosis by Arnold Levine is strongly recommended because it is full of practical advice and gives guidance to further reading. The chapter on anatomy describes, with beautiful illustrations, the lymphatic system and the breast, areas already well-known to surgeons, and follows with a description of the perhaps less well-known intrahepatic anatomy. It also gives us the only operative details in the book, that of right hemi-hepatectomy. There is an excellent chapter on radiotherapy by Tom Deeley which outlines the basic principles of the subject and its relationship to surgical practice. He reminds surgeons of the need to mark residual tumour with metal clips at the time of operation and points out the hazards of operating on tissues previously irradiated to a high dose. He stresses the importance of close co-operation between all who treat oncological diseases.

Cytoxic chemotherapy is the most recent and potentially most exciting branch of oncology. Despite the fact that as yet we have no clinically useful drugs that are cancer-specific and non-toxic, it is in this field that advances are most likely to be found in the near future. It is, therefore, disappointing that this chapter is so uninspiring. Little mention is made of the important advances in the management of childhood tumours and Hodgkin's disease which have come about following a joint approach by physicians, surgeons, radiotherapists and chemotherapists. The value of adjuvant chemotherapy in so called "early" breast carcinoma is not proven but it is certainly of interest to surgeons and warrants discussion.

The editor's contributions include an enthusiastic survey of the science and art of oncology and a chapter on the rehabilitation of the cancer patient. He makes clear that the role of the surgical oncologist is not confined to the theatre and surgical ward but extends to include total care of the patient, support of his family and education of the population at large.

Surgeons in the last century developed radical operations for malignant tumours thought to be "early". Today surgeons question the concept of "early" totally resectable cancer and work as part of a team. The useful surgical oncologist now is the one who does the right thing at the right time, be it radical or not.

Few will read this book from cover to cover, but oncologists, surgical and other, will find parts of interest.

Thelma Bates.

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The radiation dose to patients from EMI brain and body scanners

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ABSTRACT

Absorbed doses throughout the head of a Rando standard man phantom have been measured during simulated neurological examinations with the EMI Mk I brain scanner and the second generation CT 1010 brain scanner. Similar measurements have been made with the CT 5005 whole-body scanner which have also included scans through thoracic and abdominal sections of the phantom. Lithium borate thermoluminescent dosimeters placed at regular intervals throughout, and on either side of the scanned volume, have enabled estimates to be made of the total energy imparted to the phantom by each scanner as well as the absorbed dose at various locations including organs of interest in health physics such as the lens of the eye, thyroid and gonads. Isodose curves have been plotted for the central transverse section of each simulated examination. Results are reported for both the standard and high accuracy scan speed options on the two scanners where this choice is available.

It would appear that all three machines when operated at their standard scan speeds impart no more energy to the phantom than that associated with a few conventional radiographs of the same part of the body. Maximum skin doses vary from 30 to 56 mGy (3.0 to 5.6 rad) being highest for the CT 1010 scanner. Use of the high accuracy scan option increases the energy imparted and the maximum skin doses by a factor of about five, while providing much enhanced tissue density discrimination. In the case of the body scanner this higher value of energy imparted becomes comparable to that associated with lengthy fluoroscopic examinations like barium enemas.

Recent work by EMI involving further refinements to the collimation system has reduced the dose levels by typically 50%. Some preliminary results with this new system are included to indicate the likely degree of improvement, but a detailed account will be the subject of a separate paper.

Assessments of the absorbed doses likely to be received by patients exposed to diagnostic equipment utilizing computerized tomography (CT) are appearing in the literature with increasing frequency as the use of this technique becomes more widespread. Perry and Bridges (1973) carried out the first measurements of the likely exposure, following a single scan with an EMI Mk I brain scanner, using an ionization chamber and a water-filled football bladder to simulate the head. More recently Horsley and Peters (1976) reported the effect of increasing the number of scans on the exposure at the surface of a Rando head phanton. Papers have since appeared describing the dose distribution inside such head phantoms as a result of multiple contiguous scans using the EMI Mk I brain scanner (Villafana *et al.*, 1978) and the EMI CT 5000 scanner (McCullough *et al.*, 1976). Doses are reported in this paper that generally confirm the values found by previous authors and indicate that a high degree of reproducibility is possible with these scanners even when measurements are made on machines installed in different countries.

We have extended these measurements to include data on the second generation CT 1010 brain scanner and also the CT 5005 body scanner when used for neurological, thoracic and abdominal examinations. The X-ray beam geometry and the scanning sequence in this new range of scanners are markedly different from those used in the Mk I brain scanner and significantly affect the dose distribution in the phantom.

An extensive series of measurements was originally made on one of the early CT 5000 body scanners. Beam profile measurements had indicated that the X-ray beam collimation in the direction perpendicular to the scan plane was not adequate on these early machines and the large doses that were measured in the phantom when nominally contiguous slices were scanned confirmed that considerable overlap of the penumbral regions of the beam was occurring. Consequently a beam splitting plate was designed to reduce the width of the penumbra and hence the amount of overlap between adjacent scans. This device is described in more detail later but it is convenient to say here that it effectively reduced the absorbed doses in the phantom by a factor of about two for those examinations involving multiple contiguous scans. All subsequent models of EMI body scanner incorporate this device and it has also been fitted to all earlier CT 5000 scanners. Consequently no data are included for the now obsolete CT 5000 body scanner without the beam splitting plate. A few recent results relating to a further modification of the pre-patient collimator on

TABLE I

Scanning parameters for the three EMI machines studied

	Mk I Brain Scanner	CT 1010 Brain Scanner	CT 5005 Body Scanner
Beam geometry	Single pencil	Fan shaped	Fan shaped
Angular motion	180/225 deg in 1 deg steps	180/225 deg in 3 deg steps	180 deg in 10 deg steps
Standard scan time	4.5 min	1 min	20 sec
High accuracy scan time	—	4 min	70 sec
Total axial beam width at centre of rotation	37 mm	28 mm	27 mm
Recommended axial displacement between contiguous scans	26 mm	20 mm	13 mm

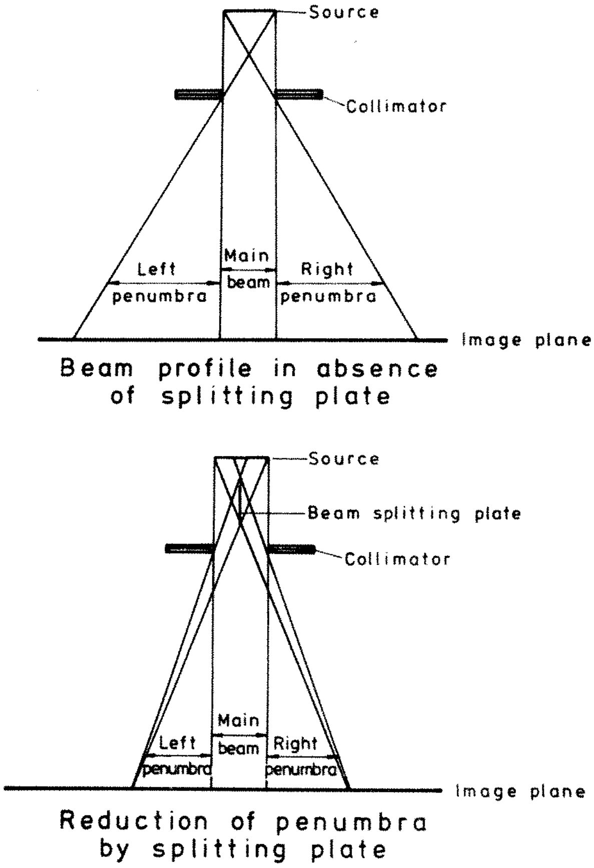
the CT 5005 scanner are included as an indication of the continuing efforts to reduce the dose received by the patient.

Operating Principles of EMI CT Scanners

A very brief description will be given of the X-ray beam geometries and the scanning motions used in the three types of machine investigated, so that the different dose distributions observed may be more easily understood. The interested reader may find more detailed information on the principles of CT scanning in the many EMI brochures promoting these machines or in the medical literature (*e.g.* Brooks and Di Chiro, 1976; McCullough *et al.*, 1976).

Table I summarizes the relevant parameters of the three EMI scanners which we have studied. They all employ the same basic scanning technique which is to make repeated linear traverses of a thin transverse slice of the patient with a small angular displacement between each traverse. The Mk I scanner uses a narrow pencil-shaped beam with essentially a single detector that requires 1 deg steps between each traverse. The second generation machines use fan-shaped beams with multiple detector arrays that allow larger rotations to be made between each traverse. A total angular displacement of 180 deg is required to obtain sufficient transmission measurements through the slice for reliable image reconstruction. The later machines complete this 180 deg rotation in fewer steps with the consequent reductions in scan time shown in Table I. However, since picture quality is necessarily related to the number of X-ray photons reaching the detectors, tissue density discrimination may be improved by increasing the scan time. Consequently a longer, high accuracy scan time option is available on the second-generation machines and the radiologist has to assess whether superior picture quality is needed and is unlikely to be marred by the increased opportunity for involuntary movement of the patient. The results of our measurements, described in this paper, indicate that the substantial increase in dose that accompanies the use of this option is a further factor that the radiologist should take into account.

Accurate beam collimation in a plane perpendicular to the slice being scanned is difficult to achieve on all three machines because of the finite extent of the X-ray tube focal spot. A diverging penumbra is unavoidable as the first part of Fig. 1 illustrates. The total beam width at the centre of rotation including this penumbra is shown in the fifth row of Table I for each machine. The relatively narrow beam on the CT 5005 has been achieved by the introduction of a beam splitting plate whose function is shown diagrammatically in the second part of Fig. 1. In order to obtain images of nominally contiguous slices an axial displacement of the patient corresponding to the full width of the beam at half maximum (FWHM) is selected (see last row of Table 1). This results in a total beam width that is somewhat larger than the displacement of the patient. Consequently there will be significant overlap of the penumbral regions of the beams used for two successive scans, particularly on the side of the patient remote from the X-ray tube where the beam will be wider than at the centre of rotation. This overlap together with the effect of scattering within the body results in considerably higher doses in the scanned volumes for multiple scans than for single scans.



Beam profile in absence of splitting plate

Reduction of penumbra by splitting plate

FIG. 1.

The action of the beam splitting plate in a plane perpendicular to the transverse scanned section.

Comparisons of the dose distributions produced by the three scanners are complicated by the fact that in the Mk I machine the X-ray tube moves around the right hand side of the patient's head, in the CT 1010 it moves around the back of the head, while in the CT 5005 it moves predominantly over the anterior surface of the patient. The isodose curves obtained on each machine clearly reflect these differences. Further differences occur in the nature and extent of the material used to surround the sections of the patient that are being scanned. Picture artefacts are likely to occur at air-tissue interfaces so these are eliminated in the Mk I scanner by a water-filled box enclosing the top of the patient's head. In the other scanners bags of tissue-equivalent bolus, approximately 10 mm thick for the CT 1010 and 20 mm thick for the CT 5005, are wrapped around the section being scanned. These provide varying amounts of pre-patient attenuation so care was taken to use them at all times in our measurements to comply with normal practice.

MEASUREMENT TECHNIQUES

The patient has been simulated by a standard-man Rando phantom and absorbed doses have been measured within and around the surface of this phantom using suitably encapsulated lithium borate thermoluminescent powder. The performance and characteristics of this dosimetry system have been described elsewhere (Langmead and Wall, 1976). It has been specially developed for medical dosimetry where its close tissue-equivalence and high precision enable doses down to 0.1 mGy (10 mrad) to be measured with an overall uncertainty of less than ±15%. The Rando phantom is made of a muscle-equivalent synthetic rubber and contains a complete human skeleton, lung-equivalent material and airways corresponding to the maxillary sinuses, the nasopharynx and the trachea. It is divided into 25 mm thick transverse sections each containing a 3 cm × 3 cm matrix of holes for accommodating dosimeter capsules or tissue-equivalent plugs. The dosimeter capsules are designed to hold about 35 mg of lithium borate powder at the centre of the transverse section. This keeps the sensitive volume of the dosimeter away from the gap between two sections where the radiation field might be perturbed by X-rays passing along the gap with inadequate attenuation.

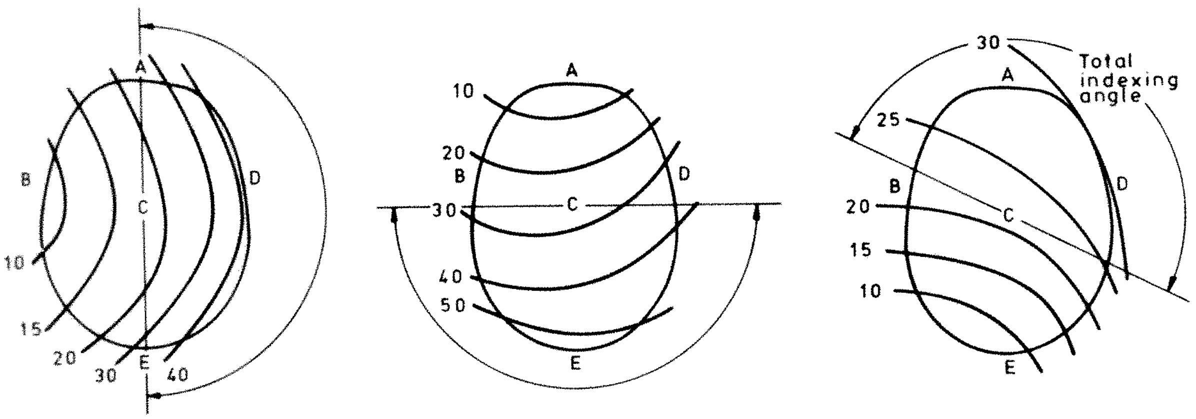
The complete phantom extending from the top of the head to 20 cm below the groin was positioned in the scanners in the standard clinical manner for each exposure. The main series of measurements were made on scanners at the end of the EMI production line immediately before despatch to customers. A few measurements were repeated on two CT 5005 scanners installed at the BUPA Medical Centre, London, and at Manchester University Medical School, to check the reproducibility of the results. Neurological examinations were simulated with each type of scanner, by obtaining images of eight contiguous transverse slices of the head of the phantom from just below the infra-orbital line to within 2.5 cm of the top of the skull. This required four separate scans with the Mk I brain scanner and the CT 1010 which obtain data for two 13 mm thick slices per scan. The CT 5005 machine with its much faster scan time can afford to examine a single slice per scan and therefore requires eight separate scans to cover the same area. Thoracic and abdominal examinations were simulated with the CT 5005 body scanner in a similar manner by performing eight contiguous scans centred on transverse sections through the nipples and the lower costal margin respectively.

All scans described in this paper were conducted with the X-ray tube operating at a potential of 140 kV with a current of 28 mA. Settings of 120 kV and 32 mA are more usually employed for brain scans but it was considered desirable on this occasion to keep the settings constant for all examinations and to use those likely to result in the highest dose. Villafana *et al.*, (1978) have found a general reduction of around 25% in the doses received by a Rando phantom from a Mk I brain scanner when operated at 120 kV rather than 140 kV. Consequently it would be reasonable to reduce the doses quoted in this paper for brain scans by 25% if operation at 120 kV was guaranteed.

The absorbed dose has been measured at a number of uniformly distributed points throughout the phantom section lying at the centre of the scanned volume for each simulated examination. In addition dosimeters placed within the scanned slice and in the two sections lying on either side of the scanned slice for single scans have enabled us to determine the extent to which the diverging beam and scattered radiation expose closely surrounding tissue. Radiation scattered to organs of particular interest in radiological protection, such as the lens of the eye, thyroid and gonads, have also been monitored.

Results

Sufficient measurements were obtained in the slice lying at the centre of each volume examined for



Mk I CT1010 CT5005

Fig. 2.

Isodose curves in the central transverse plane of the irradiated volume for simulated brain examinations of eight contiguous slices with each scanner operated at the standard scan speed. Anterior is at the top of the diagram. The numbers indicate absorbed dose in mGy (10 mGy = 1 rad).

TABLE II

Absorbed doses in the head for simulated brain examinations with the three types of EMI CT scanner operated at their standard and high accuracy scan speeds. Each examination provided data for eight contiguous slices. Figure 2 shows the positions of the dosimeters (10mGy = 1 rad).

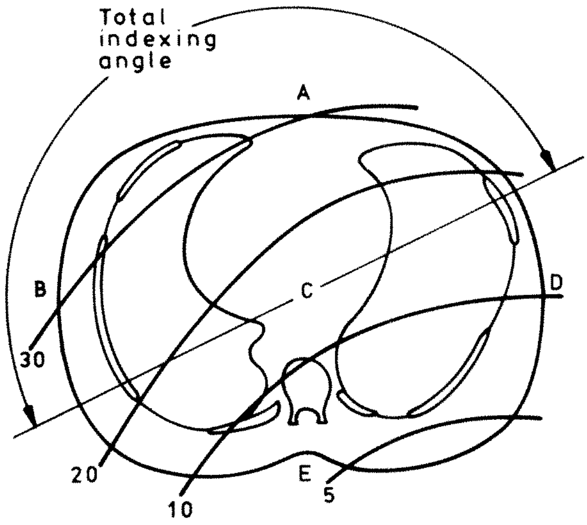
	Absorbed dose per examination (mGy)					
	Mk I		CT 1010		CT 5005	
Dosimeter position	Standard scan	High accuracy	Standard scan	High accuracy	Standard scan	High accuracy
A	25	not available	8.2	57	28	120
B	6.7		28	180	23	110
C	19		26	130	21	100
D	42		38	160	30	160
E	34		56	340	9.4	42
Eye lens (left)	18		4.8	54	27	85
Eye lens (right)	28		4.8	53	27	67
Thyroid	1.4		0.5	2.4	0.6	1.9

crude isodose curves to be constructed. The resolution was not adequate for demonstrating local perturbations caused by bone or lung-equivalent material in the phantom but the general trend of the dose distribution has been established. Figure 2 shows how these isodose curves differ between the three types of scanner for our simulated brain examinations using the standard scan speed on each machine. Doses measured at the positions labelled A to E in Fig. 2 are shown in Table II together with the increased dose at these positions that results from the use of the high accuracy scan-speed options available on the CT 1010 and CT 5005 machines. Increasing the value of the isodose curves in Fig. 2 by a factor of five provides a good estimate of the dose distribution to be expected from use of the slower scan speed option. The doses received by the thyroid and the lenses of the eyes from these neurological examinations are also given in Table II. Ovaries and testes have not been included because the dose to these organs was too low (less than 0.1 mGy) to be measured accurately for all scans through the brain.

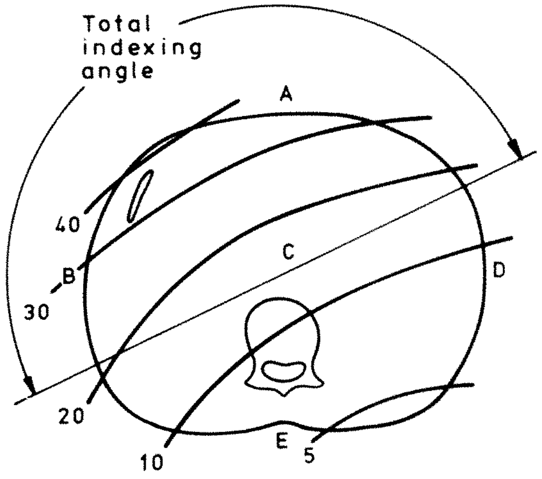
The maximum doses received by the head from each type of scanner have been underlined to make them stand out more clearly in the Table. Comparing these figures alone the standard scan-speed options of the CT 1010 and the CT 5005 produce maximum skin doses that are respectively 33% above and 30% below that from the Mk I scanner, none of them exceeding 60 mGy (6 rad). The high accuracy scan on the the CT 1010 however results in a maximum skin dose of 340 mGy (34 rad) while for the CT 5005 it has been kept down to approximately half this value.

Dose contours for thoracic and abdominal examinations using the CT 5005 body scanner at its standard scan speed are shown in Fig. 3. Doses at individual points within the central slice and at the thyroid, ovaries and testes are indicated in Table III in a similar manner to Table II. The isodose curves are skewed towards the phantom's left for the thoracic and abdominal scans in contrast to the brain scan with the CT 5005 shown in Fig. 2 where they are skewed to the right. This is because the phantom was inserted head first into the scanner for the brain scan but feet first for the other two scans. The resulting orientation of the total 180 deg indexing angle, which commences 25 deg below the horizontal, is shown on each section in Figs. 2 and 3.

Reference to the data in Table III will show that multiplying these doses by a factor of about four provides a good indication of the dose distribution to be expected from multiple scans carried out at the slow, high resolution, scan-speed option. It may seem surprising that an increase in total scan time by a factor of 3.5 should result in an increase in dose by a higher factor. However, it should be remembered that the X-ray tube turn-around and indexing times occupy a significant percentage of the total period for a fast scan, and these remain unchanged



Thorax



Abdomen

FIG. 3.

Isodose curves in the central transverse plane of the irradiated volume for simulated thoracic and abdominal examinations of eight contiguous slices with the CT5005 operated at the normal scan speed. The numbers indicate the absorbed dose in mGy (10 mGy = 1 rad).

TABLE III

ABSORBED DOSES IN THE TRUNK FROM SIMULATED EXAMINATIONS WITH THE CT 5005 SCANNER OPERATED AT THE STANDARD AND HIGH ACCURACY SCAN SPEEDS. EACH EXAMINATION COMPRISED EIGHT CONTIGUOUS SCANS. FIGURE 3 SHOWS THE POSITIONS OF THE DOSIMETERS (10 mGy = 1 RAD).

	Absorbed dose per examination (mGy)					
	Thoracic examination		Abdominal examination		Modified collimator, thorax	
Dosimeter position	Standard scan	High accuracy	Standard scan	High accuracy	Standard scan	High accuracy
A	33	120	33	130	16	50
B	31	120	33	130	11	33
C	15	59	17	88	—	—
D	12	50	10	37	4.4	15
E	7.2	28	6.3	26	3.7	12
Thyroid	2.0	6.6	0.1	0.4		
Ovaries	0.1	0.3	0.6	0.3		
Testes	0.2	0.2	0.5	1.2		

for a slow scan. The time actually spent traversing the head will consequently be increased by a factor greater than 3.5 for the slow scan.

The maximum skin doses from these thoracic and abdominal examinations are similar to those from neurological examinations with the CT 5005. The last two columns in Table III show preliminary results arising from experimental modifications to the pre-patient (entry) collimator of a CT 5005 scanner. A reduction in dose of approximately 50% has been achieved and is accompanied by only a marginal change in image quality, the noise level being increased by about 3 to 5%.

Reproducibility of results

Comparison of our results with those obtained by other authors would suggest that the output of different EMI Mk I brain scanners is remarkably similar. The operating parameters and measurement techniques of Villafana *et al.*, (1978) most closely match the ones that we have used and agreement to within ±12% has been achieved in our respective dose estimates at nearly every measurement point within our standard Rando phantom. We have tested the reproducibility of our dose estimates for CT 5005 scanners by making repeat measurements on the same scanner under identical operating conditions and on three different scanners of the same type installed in Hayes, London and Manchester. Repeat measurements on the same scanner showed agreement to within ±10%. The doses obtained at four positions on the phantom when examined by the three different CT 5005 machines are shown in Table IV. All measurements were in the central slice of seven contiguous scans made at the standard scan speed and were made in the area of maximum dose. The agreement is not so good as that seen with the Mk I scanner but the doses are still within ±20% of the mean for all three machines. As the doses do not vary systematically between machines, differences in output between the three X-ray tubes cannot be responsible for the variations observed. No attempt was made to monitor the X-ray tube output directly but all three machines were operated at identical settings of kV and mA. The variations are more likely to be due to small differences in dosimeter location and phantom alignment since exact positioning of the surface dosimeters and of the phantom within the CT 5005 scanners is difficult to achieve.

TABLE IV

DOSES MEASURED ON THE SURFACE OF A RANDO PHANTOM TAKEN WITH THREE DIFFERENT CT 5005 SCANNERS INSTALLED IN DIFFERENT TOWNS IN ENGLAND (10 mGy = 1 rad).

	Absorbed dose per examination (mGy)		
Dosimeter location	Hayes	London	Manchester
Centre forehead	28	32	32
Right temple	30	34	26
Above right ear	30	24	23
Above left ear	23	17	23

DISCUSSION

The dose distributions in patients examined by computer-assisted tomography are obviously quite

TABLE V

Approximate estimates for the energy imparted to patients by typical examinations with EMI brain and body scanners and by other conventional diagnostic techniques.

Examination	Technique	Approximate energy imparted (mJ)	Reference
8 slices of brain	CT 5005, fast	50	
	CT 5005, slow	250	
	CT 1010, fast	73	
	CT 1010, slow	360	
	EMI Mk I	56	
8 slices of torso	CT 5005, fast	100	
	CT 5005, slow	500	
Skull	Single radiograph	30	Perry and Bridges, 1973
Lung	Full size radiography	21	Bengtsson *et al.* 1976
Lung	Photofluorography	73	Bengtsson *et al.* 1976
Stomach	Barium meal	310	Bengtsson *et al.* 1976
Colon	Barium enema	600	Bengtsson *et al.* 1976

different from those associated with conventional radiography and fluoroscopy. Attenuation across the body is far less from a multidirectional source of X rays spanning 180 deg than from a diverging beam incident in only one direction. Skin dose measurements or dose measurements at only a few anatomical locations rarely provide an adequate indication of the relative somatic risks associated with the two modalities. A more useful quantity for comparing the general somatic effects of different dose distributions may be the total energy imparted to the patient. Only a rough approximation to this quantity can be derived from the present data because of the lack of detailed knowledge of the dose distribution throughout the phantom. The energy imparted to the scanned volume alone can be calculated by multiplying the mass of each phantom section that falls within the scanned volume by the average dose to that section and by summing the products. The average doses derived from our data for the CT 1010 and CT 5005 are unlikely to be the true average doses to the sections because the limited number of measurement points were not necessarily uniformly distributed with respect to the dose distribution. However more detailed measurements made on the Mk I brain scanner, where 28 uniformly distributed dosimeters were used in each brain section instead of only nine, suggest that the average dose computed from the smaller number of measurements is unlikely to be more than 20% different from the more accurate average dose calculated from 28 measurements.

The energy imparted to the 25 mm thick sections on either side of the scanned volume can be estimated from the additional dose measurements that were made during single scans on each machine. The average dose to the immediately adjoining sections was found to be 40%, 18% and 11% of the average dose to the scanned section for the Mk I, CT 1010 and CT 5005 scanners respectively. These values reflect the differences in beam width between the scanners and hence the amount of beam overlap into surrounding tissue.

Using these assumptions approximate values for the energy imparted to the phantom up to 25 mm from the edge of the scanned volume for our simulated clinical examinations have been calculated and appear in Table V. It is furthermore assumed that the energy imparted to more remote parts of the phantom is negligible. The Rando phantom is modelled on an average man 5ft 9in tall weighing 73.5 kg. The energies imparted to patients with physiques that differ substantially from this norm are likely to be different from the values quoted.

Values for the energy imparted to patients from more conventional diagnostic techniques are rather limited at the moment. Perry and Bridges (1973) calculated a value of the order of 30 mJ for the energy imparted by a single skull radiograph, while Bengtsson *et al.*, (1976) have measured energies imparted to patients from a variety of diagnostic examinations in Sweden. Some of these values are included in Table V to enable rough comparisons to be made of the relative somatic risk of computer-assisted tomography with more conventional techniques. Bengtsson's results represent mean values for the energy imparted in a complete examination measured by a technique developed by Carlsson (1963) at 13 Swedish hospitals between 1973 and 1975. Values for individual patients can vary by up to a factor of four from the mean, depending on the equipment and techniques employed, the physique and pathology of the patient, and the skill of the radiologist, but as long as Bengtsson's data are averaged over a representative sample of patients the mean values should be adequate for purposes of our rough comparison.

It would appear that examination of the brain with the CT 5005 operated at its fast scan speed imparts a similar amount of energy to the phantom as the Mk I scanner and the CT 1010, and is roughly equivalent to a couple of conventional skull radiographs. A fast scan of the torso imparts about twice this energy; although this is considerably more than that associated with a full size chest radiograph it only represents about a 40% increase over photofluorography of the chest. The slow, high resolution scan-speed option, on the other hand, imparts about five times the energy to the patient as the standard scan for both machines where it is available. This raises the dose received by the patient in brain scans to levels similar to those associated with conventional examinations like barium meals which involve a moderate amount of radiography and fluoroscopy. For body scans the energy imparted rises to levels approaching those for lengthy screening examinations like barium enemas. It should be appreciated, of course, that the conventional examinations that the brain scanners are most likely to replace do involve very extensive fluoroscopy and radiography. No data could be found for the energy imparted by cerebral angiography or pneumoencephalography, but comparison of the skin doses resulting from these examinations with that from barium enemas would suggest that they are likely to impart at least as much if not more energy to the patient.

Computer-assisted tomography would therefore seem to offer unique diagnostic information at levels of somatic risk similar to those currently accepted in conventional diagnostic radiology. It should be appreciated, however, that selection of the high accuracy scan-speed option does raise the dose received by the patient to levels that approach the top end of the conventional diagnostic range and consequently the need for improved picture quality should be fully justified for each patient before they are exposed to the associated increase in risk of somatic injury.

Further improvements in the pre-patient collimator show promise in reducing the dose to the patient without seriously affecting picture quality.

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REFERENCES

Bengtsson, G., Blomgren, P., Bergman, K., and Aberg, L. 1976. Patient exposures in Swedish diagnostic radiology. *Swedish National Institute of Radiation Protection*, SSI: 1976–2013.

Brooks, R. A., and Di Chiro, G., 1976. Principles of computer assisted tomography (CAT) in radiographic and radioisotopic imaging. *Physics in Medicine and Biology*, *21*, 689–732.

Carlsson, C., 1963. Determination of integral absorbed dose by exposure measurements. *Acta Radiologica, Therapy*, *1*, 433–458.

Horsley, R. J., and Peters, V. G., 1976. Radiation exposure from EMI scanner–multiple scans. *British Journal of Radiology*, *49*, 810–811.

Langmead, W. A., and Wall, B. F., 1976. A TLD system based on lithium borate for the measurement of doses to patients undergoing medical irradiation. *Physics in Medicine and Biology*, *21*, 39–51.

McCullough, E. C., Payne, J. T., Baker, H. L., Hattery, R. R., Sheedy, P. F., Stephens, D. H., Gedgaudus, E., 1976. Performance evaluation and quality assurance of computed tomography scanners, with illustrations from the EMI, ACTA and Delta scanners. *Radiology*, *120*, 173–188.

Perry, B. J., and Bridges, C., 1973. Computerised transverse axial scanning (tomography): part 3. Radiation dose considerations. *British Journal of Radiology*, *46*, 1048–1051.

Villafana, T., Scouras, J., Leland, K., McElroy, N., and Paras, P., 1978. Health physics aspects of the EMI computerised tomography brain scanner. *Health Physics*, *34*, 71–82.

1979, *British Journal of Radiology*, *52*, 197–208

The fixed horizontal neutron therapy beam at Edinburgh: dosimetry and radiation protection

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ABSTRACT

A compact cyclotron producing 15 MeV deuterons has been installed at the Western General Hospital, Edinburgh, to extend the Medical Research Council's clinical trials of fast neutrons. Two treatment rooms are available one of which has an isocentric unit and the other a fixed horizontal beam which is the subject of this paper. A radiation protection survey has demonstrated safe levels of radiation throughout the building although there is some activation of the fixed horizontal beam cone resulting in doses to radiographers of 10 mrem per week. The calibration of neutron dose is discussed and the measurements of dose distribution described. Isodose and depth-dose data for both the neutron and photon components of the field are presented.

Fast neutrons have been used in the control of malignant disease at the Medical Research Council's Cyclotron Unit, Hammersmith Hospital, London, since 1966. Catterall (1974) presented observations on patients who had received fast neutron radiotherapy between 1969 and 1974 for advanced "radio-resistant" or recurrent tumours of various sites, whilst Catterall *et al.*, (1975) reported the results of a clinical trial of fast neutrons for the treatment of advanced tumours of the head and neck. Recently Catterall *et al.*, (1977) have shown that the benefit that was previously reported has been maintained. However, in 1973, before these analyses had been completed, the results of fast neutron therapy were sufficiently encouraging for the Medical Research Council, with support from the Cancer Research Campaign and the Scottish Home and Health Department, to approve the establishment of a new facility at the Western General Hospital, Edinburgh, specifically for fast neutron therapy and to be operational in three years. Detailed studies showed that the only fast neutron source which could be guaranteed as a practical therapeutic tool was a cyclotron and that a commercial compact cyclotron was available which could be installed in time to meet the schedule.

At Hammersmith, treatments have been hampered by poor penetration (approximately 9 cm 50% depth dose) and a single fixed horizontal beam. Available funds did not permit a higher energy machine at Edinburgh but did allow the provision of a steerable neutron beam and two treatment rooms. The steerable isocentric neutron facility offered commercially was of an untried design; to guarantee meeting the date for the start of therapy, a fixed horizontal beam duplicating that at Hammersmith was provided in one of the treatment rooms. This would allow for some further development time, if that were needed, to bring the new isocentric design into operation.

The equipment chosen was the model CS30 cyclotron manufactured by the Cyclotron Corporation, Berkeley, California, USA, which is designed to accelerate protons to 28 MeV, deuterons to 15MeV, helium−3 ions to 40MeV and helium −4 ions to 30 MeV. For the production of fast neutrons the deuteron beam is used with a beryllium target. The beam transport system includes a switching magnet so that the deuteron beam may be directed either into the treatment room containing the fixed horizontal neutron beam facility, or into that containing the isocentric steerable neutron beam equipment. The maximum beam current which can be achieved on either target is 100 μA.

The first patients were treated with the fixed horizontal beam in March 1977, three years and two months from the completion of the plans for both the building and the cyclotron. This paper describes the initial radiation protection and dosimetric work carried out before commencement of treatment of patients with the fixed horizontal beam. Detailed considerations of the isocentric unit will be the subject of a later publication, although provisional data have been presented by Williams *et al.* (1978).

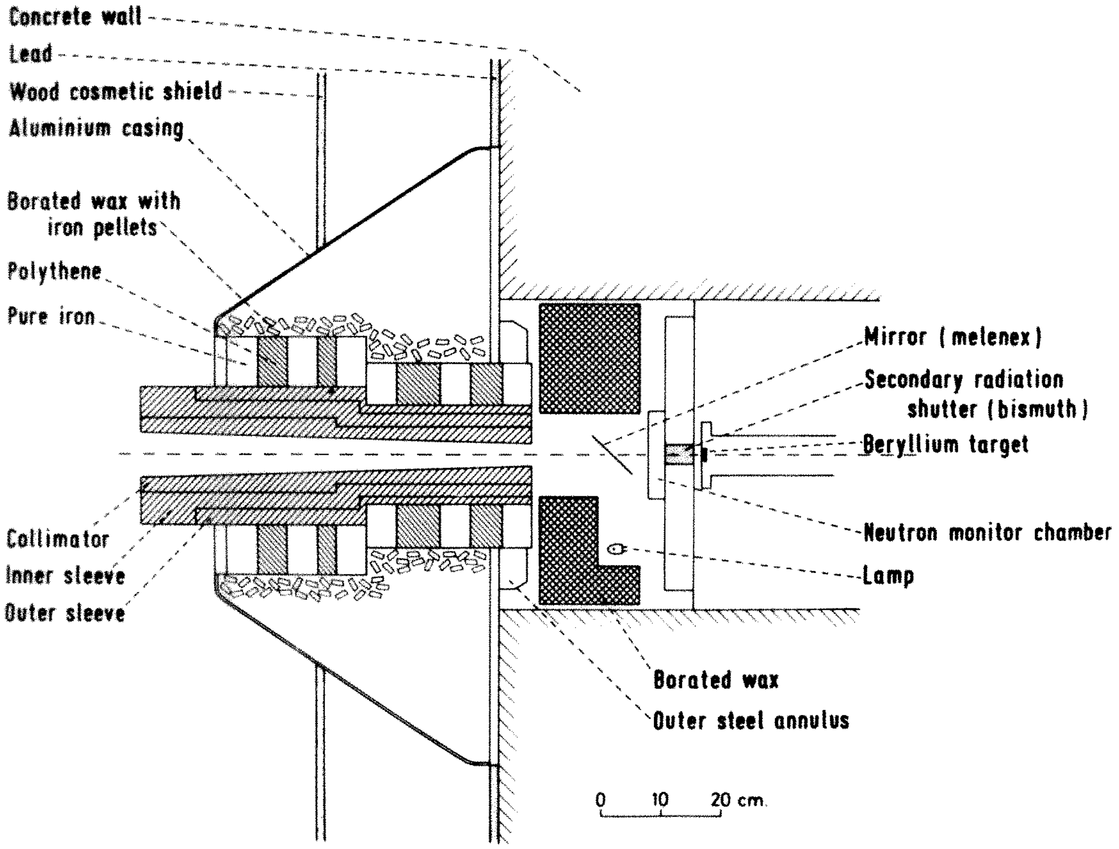

FIG. 1.
The fixed horizontal beam cone.

FIXED HORIZONTAL BEAM

The design of the fixed horizontal beam is shown in Fig. 1 and is a modified version of that used at Hammersmith (Bewley & Parnell, 1969 Bewley, 1970). In the shielding, use is made of hydrogenous materials and high purity iron. Iron is used to reduce the energy of high energy neutrons by inelastic scattering, and hydrogenous materials are used to attenuate lower energy neutrons by elastic scattering with the hydrogen nuclei. In selecting the iron, care was taken to minimize the levels of non-ferrous materials in an attempt to reduce the radiation exposure of personnel due to induced radioactivity in the shield. In particular manganese was avoided as the thermal-neutron capture reaction ^{55}Mn (n, γ) ^{56}Mn for which the cross section is large (about 13 barn) produces a product which decays with a half life of 2.58 hours and emits gamma radiations with energies of 0.85, 1.81 and 2.11 MeV. The shielding adjacent to the aperture into which the interchangeable collimators are inserted consists of alternate layers of polythene and iron, the design being based on measurements of the attenuation properties of multilayer shields for 14 MeV neutrons as described by Greene and Thomas (1969) and Maruyama and Bouts (1972). The remainder of the cone is filled with pellets of iron embedded in borated paraffin wax.

Following installation of the shielding cone three further measures were taken in order to reduce the levels of induced activity in the cone and the resulting dose to personnel working in the treatment room.

(i) The remaining space around the monitor ionization chamber and field light assembly within the cone was filled with paraffin wax and boric acid to provide extra attenuating material between the target and the shielding cone.

(ii) The wall area surrounding the cone was covered with lead 1.25 cm thick and the back plate of the cone with lead 2.5 cm thick to provide shielding against any activity induced in the concrete at the edge of the cone.

(iii) A panelled wood cover was installed to improve the appearance of the room and to increase the distance of personnel from any induced activity in the cone.

Patients are treated at 125 cm FSD with the distance from the end of the collimator to the surface of the patient being 33 cm. The field size is defined by interchangeable collimators manufactured from high density compressed wood. Two types of material have been used: Japroc N (Permali) and Benelex (Masonite Corporation). Both materials have a density of 1.39 g cm^{-3} and there is no significant difference in their beam defining properties. To achieve the required attenuation each collimator is 64 cm long, and in order to construct a collimator large enough to define a field size of 21 × 21 cm at the treatment distance, an end diameter of 23 cm is required. If a cylindrical collimator were produced to define the smallest field size required (6 × 6 cm), the total weight of the collimator would be 36 kg. To reduce this weight to a more manageable level an interlocking system of collimators and sleeves has been devised as shown in Fig. 1.

The housing into which the collimators fit has two cross-sections, the outer section having a diameter of 23 cm and the inner section, which is 27 cm long, having a diameter of 13.5 cm. The largest collimators, which are those defining a field size with an area greater than 330 cm^2, fit directly into the housing. Intermediate collimators, which define fields with areas between 122 cm^2 and 330 cm^2, fit into an outer sleeve of collimator material which can be placed into the collimator housing separately. Small collimators for field areas less than 122 cm^2 require a second sleeve which fits into the outer sleeve. In this way the individual sleeves and collimators weigh less than 19 kg (21 × 21 cm field) and the small collimators weigh approximately 7 kg. At present, 12 sizes of collimator are available which can also be used in the isocentric unit. To increase the total number of field sizes which can be used, collimator inserts are provided. These are tapered sections of compressed wood which fit down the edge of the collimator thus effectively reducing the field size.

Wedge filters are also available. These are constructed of polythene containing approximately 0.5% of boron. They are positioned at the treatment end of the collimator system and there is an interlock system which requires the radiographer to confirm the wedge angle at the control desk before treatment can commence. Three wedge angles are available which are nominally 25, 35, and 45 deg. The wedges reduce the dose-rate by factors ranging from 1.83 for the 25 deg wedge to 2.72 for the 45 deg wedge. These wedge factors were considered to be inconveniently high and in order to reduce them for the small collimators a second set of wedges were made having lower wedge factors which are 1.64 for the 25 deg wedge and 2.03 for the 45 deg wedge. The wedge holders have been designed so that it is not possible to fit the wrong wedge to a given collimator.

RADIATION PROTECTION

Figure 2 shows a plan of the building which is sited as an extension to the Radiotherapy Institute of the Western General Hospital. The basic shielding around the cyclotron and treatment rooms consists of concrete walls two metres thick. Some parts of the labyrinth walls are thinner, but the total shielding is at least two metres. The entrance to each labyrinth is protected by a barrier which is interlocked with the cyclotron control system.

Neutrons are produced in each room by bombarding a thick beryllium target with 15 MeV deuterons. For the fixed horizontal beam this target is located in the wall separating the treatment room from the cyclotron vault whilst for the isocentric unit the target is located in the shielding assembly which forms part of the rotating gantry.

Following the installation of the cyclotron and the commissioning of the two beam lines, a survey of stray radiation levels around the unit was undertaken using two different operating conditions. First the deuteron beam was incident upon an aluminium beam stop located immediately in front of the switching magnet, a condition which produced maximum radiation levels within the vault. Radiation measurements were made in areas adjacent to the vault on the ground floor, in the basement beneath the cyclotron control room and in the first floor plant room located above parts of the treatment rooms and cyclotron vault. Second, during neutron production in one treatment room, radiation measurements were carried out in the areas adjacent to the treatment rooms and in the room not in use.

Measurements were carried out using a β–γ dose-rate meter type 0500 (Nuclear Enterprises Ltd.) and a neutron dose-equivalent rate meter type NM1 (Nuclear Enterprises Ltd.). In addition, following the commencement of fast neutron therapy, doses accumulated during a four week period were determined at various locations around the unit using β–γ film badges and fast neutron track emulsions supplied and processed by the National Radiological Protection Board.

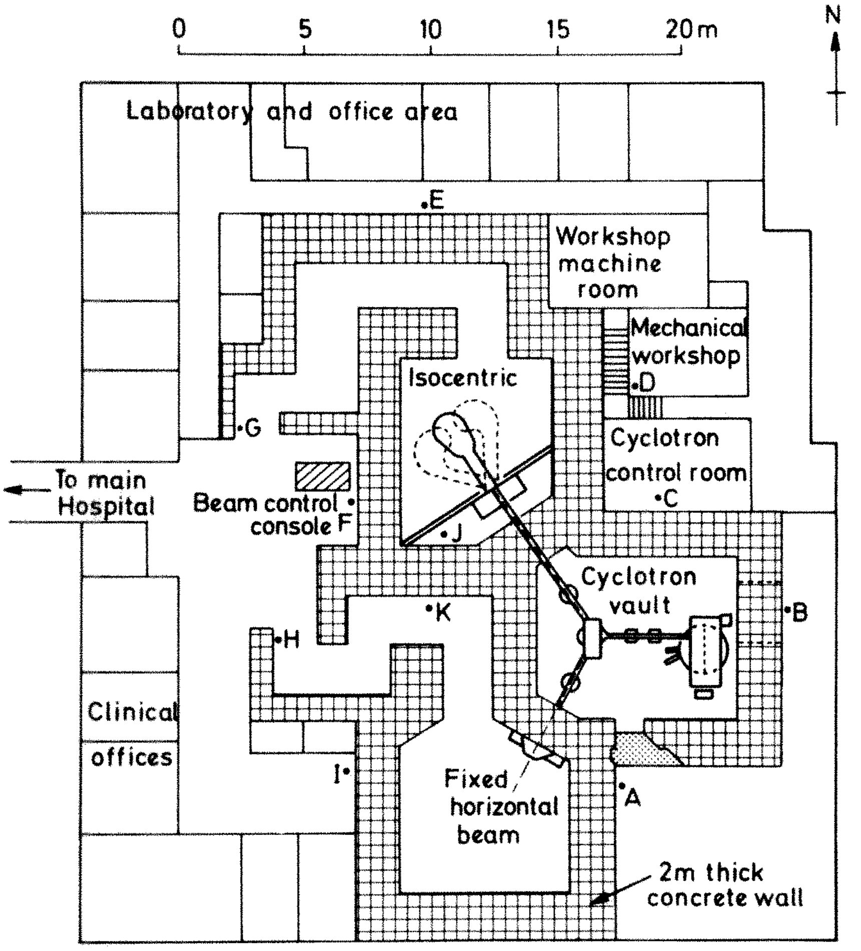

FIG. 2.

Ground floor plan of the Cyclotron Unit showing the positions of the radiation survey.

The initial survey showed that no neutron radiation greater than 0.1 mrem/h could be detected in the building during cyclotron operation, with the exception of levels of approximately 0.25 mrem/h at the entrances to the two treatment rooms. These levels were confirmed by the accumulated neutron dose measurement. The results of the initial γ-ray dose-rate measurements integrated over a period of 40 hours, the estimated time the cyclotron was operational during the survey period, are shown in Table I. Dose-equivalents of less than 0.02 rem were recorded by the film badges in all the positions which could be surveyed showing a good agreement between the two sets of results. The difference in dose levels at the vault door occurred because the dose-rate measurements were made with the beam incident on the beam stop which is situated directly behind the door, while during a four week period only a small fraction of time is spent in this condition. These results indicate that the radiation levels within the building are well within the limits for occupationally exposed workers.

Activation of the materials in the cone and the other areas close to the neutron target does cause some exposure to personnel working within the treatment room. During the first six months of treatment the dose to radiographers involved in the fast neutron therapy programme was approximately 0.12 mrem per field treated, with the average weekly dose being 10 mrem. No measureable build-up of long-lived radioactivity in the shielding cone was observed during this period.

TABLE I

GAMMA RADIATION LEVELS AROUND THE MRC CYCLOTRON UNIT, EDINBURGH

Position	Initial dose-rate integrated over 40 hr (rem)
A. Vault door	0.06
B. Vault wall	0.01
C. Control room	0.01
D. Mechanical workshop	< 0.004
E. North corridor	< 0.004
F. Beam control console	0.01
G. Entrance to isocentric treatment room	0.01
H. Entrance to fixed horizontal beam treatment room	0.02
I. Patients waiting area	< 0.004
J. Isocentric treatment room wall (south)	0.02
K. Fixed horizontal beam treatment room wall (north)	0.02
Basement	0.02
Plant room (1st floor)	< 0.004

DOSIMETRY METHODS

Fast neutron dosimetry is complicated by the presence of photons produced by interactions in the target, the collimator and the patient or other scattering media. The contribution of photons to the total absorbed dose varies between approximately 3% in air on the central axis of the beam to greater than 50% outside the main beam in a tissue equivalent medium. Since the RBE for neutrons and photons are very different the absorbed dose due to each component should be estimated separately. Problems of mixed beam dosimetry have been discussed in detail elsewhere (*e.g.*, ICRU 1977). The method that has been adopted here to obtain neutron absorbed dose is to measure the total dose using a homogeneous tissue-equivalent ionization chamber and to subtract the photon contribution which is measured separately with an energy-compensated Geiger-Müller counter.

The tissue-equivalent chamber used as a calibration standard is a gas-flow type with a nominal collecting volume of 0.5 cm^3 (Exradin Inc.). Both the chamber wall and the collecting electrode are made from tissue-equivalent conducting plastic, A-150, whose composition has been given by Smathers *et al.* (1977). This composition is closely matched in terms of hydrogen and nitrogen content by the gas used in the chamber, which is a mixture of methane, carbon dioxide and nitrogen, 64.4%, 32.2% and 3.4% by partial pressure respectively. During irradiation the charge produced in the chamber is measured using a digital electrometer (model 616, Keithley Instruments Ltd.). In order to measure the volume of the chamber it is calibrated in a 4 MV X-ray beam against a secondary standard dosemeter calibrated at the National Physical Laboratory, Teddington.

Following irradiation the total absorbed dose in tissue (ICRU muscle, ICRU 1964) can be calculated from the charge collected (Q_T) in the neutron beam by the following relationship:

$$(D_T)_t = \frac{\overline{W}_N}{\overline{W}_c} \cdot \frac{(S_{m,g})_N}{(S_{m,g})_c} \cdot \frac{K_t}{K_m} \cdot \frac{(\mu_{en}/\rho)_m}{(\mu_{en}/\rho)_{H_2O}} \cdot \frac{X_c C_\lambda}{Q_c} \cdot Q_T$$

where subscripts N, c refer to a neutron beam and the calibration beam respectively,
subscript T refers to the mixed radiation beam,
subscripts t & m refer to tissue and the wall material of the chamber respectively,
$\overline{W}_N ; \overline{W}_c$ are the average energies required to produce an ion pair in the gas for neutrons and the calibration radiation respectively.
$(S_{m,g})_N$, $(S_{m,g})_c$ are the mass stopping power ratios of the wall to gas materials for the neutron and calibration radiations respectively.
K_t/K_m is the ratio of the kerma in tissue to the kerma in the wall material calculated for the spectrum of the neutron beam.
$(\mu_{en}/\rho)_m/(\mu_{en}/\rho)_{H_2O}$ is the ratio of the mass energy absorption coefficients in the wall material and in water for the calibration beam of photons.
Q_c/X_c is the charge collected per unit exposure in the calibration beam.
C_λ is the factor required to convert exposure to absorbed dose in water for the calibration beam.

Systematic errors in the measurement of total dose are due to the uncertainties in the constants used in this equation. Table II lists the values of these constants which have been used. It has been assumed that the chamber is homogeneous so that the ratio of the mass stopping powers of the wall and gas materials is 1.0. However, it should be noted that Sautter and Zimmerman (1965) and Williamson and Watt (1972) have shown that the mass stopping power of photons and alpha particles in hydrocarbons does depend on the physical state of the material and that $(S_{m,g})_N$ may be less than 1.0. Due to the uncertainty in these data and the lack of knowledge of the secondary particle spectrum associated with neutrons, it has been recommended that a value of 1.0 should be used at the present time (ICRU, 1977). In calculating the kerma ratio, the neutron energy spectrum has been assumed to be the same shape as that measured by Parnell (1972) with the neutron energies degraded by the ratio of the

TABLE II

Constants used in neutron dosimetry

Quantity	Value	Reference
$\overline{W}_c$	0.95	ICRU (1977)
$\overline{W}_N$		
$(S_{m,g})_c$	1.0	
$(S_{m,g})_N$	1.0	
K_t	0.972	ICRU (1977)
$\overline{K}_m$		
$\left(\frac{\mu_{en}}{\rho}\right)_m \Big/ \left(\frac{\mu_{en}}{\rho}\right)_{H_2O}$	0.992	Storm & Israel (1970)
C_λ	0.94	

energy of the deuteron beam (15 MeV) to that used by Parnell (16.7 MeV).

The Geiger-Müller counter used to measure the photon contribution is a Mullard MX163 which is surrounded by a tin/lead filter to give an approximately uniform energy response above 200 keV (Wagner and Hurst, 1961). The response of the counter to fast neutrons relative to its response to photons, k_u, is very low. Recent measurements by Hough (1977) using a modification of the lead attenuation technique described by Attix *et al.* (1975) have shown that $k_u = 0.0074 \pm 0.0007$ for neutrons produced by 16.7 MeV deuterons on a beryllium target, which is the value that has been used in this work. The photon calibration of the GM counter was made using a ^{137}Cs source.

For measurements of dose distribution in a water phantom a smaller tissue equivalent chamber was used in order to give good spatial resolution. This chamber has an approximate volume of 0.1 cm^3 (EG & G type IC18) and was used with the GM counter previously described. The GM counter has a high sensitivity to thermal neutrons and, in order to overcome this, a ^{6}Li shield was placed round the tube. ^{6}Li has a high thermal-neutron absorption cross-section and capture is not accompanied by prompt γ emission.

Measurements of depth doses and cross beam data were made in a 40×40×40 cm Perspex-walled water phantom using the computer controlled dosimetry system described by Bottrill *et al.* (1975). Some modifications of this system had to be made in order to make it suitable for use with the neutron beam rather than with high energy X rays for which it was designed. Because of the lower dose-rates and depth doses, the ionization currents encountered in the fast-neutron beam isodose measurement programme were lower than those for a high energy X-ray beam. The original equipment was found to be unsuitable at these low currents (of the order of 1 pA) so that a more stable and sensitive comparator unit was built. In addition the GM counter signal had to be converted to a signal suitable for input to the computer and to do this a ratemeter circuit was incorporated into the modified unit. Changes also had to be made to the data acquisition programme. The design of the ionization chamber and the water tank prevented measurements being made at a depth of less than 13 mm. Since the maximum dose occurs at approximately 1 mm deep the programme had to be altered to extrapolate the measurements to the surface.

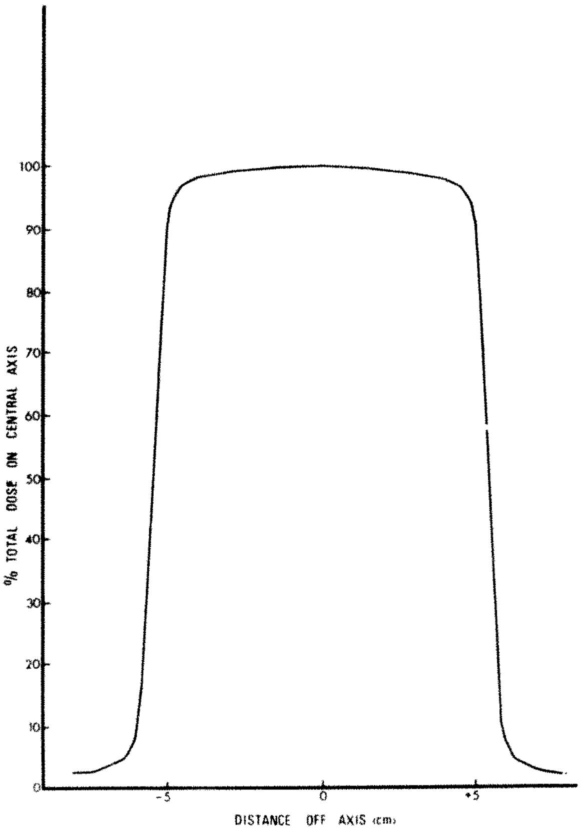

Fig. 3.

Cross plot of 11×11 cm field at 125 cm FSD in air using a tissue equivalent ionization chamber.

The total time required to measure the data for each field condition was greater than the average of three minutes reported by Bottrill *et al.* (1975) for a linear accelerator. They used sampling times of approximately 200 ms at each data point, which gives an overall measurement time for each field of 34 s. This is small compared with the time taken to move the chamber to each point together with a 250 ms pause before sampling to allow for the response time of the dose measuring system. For

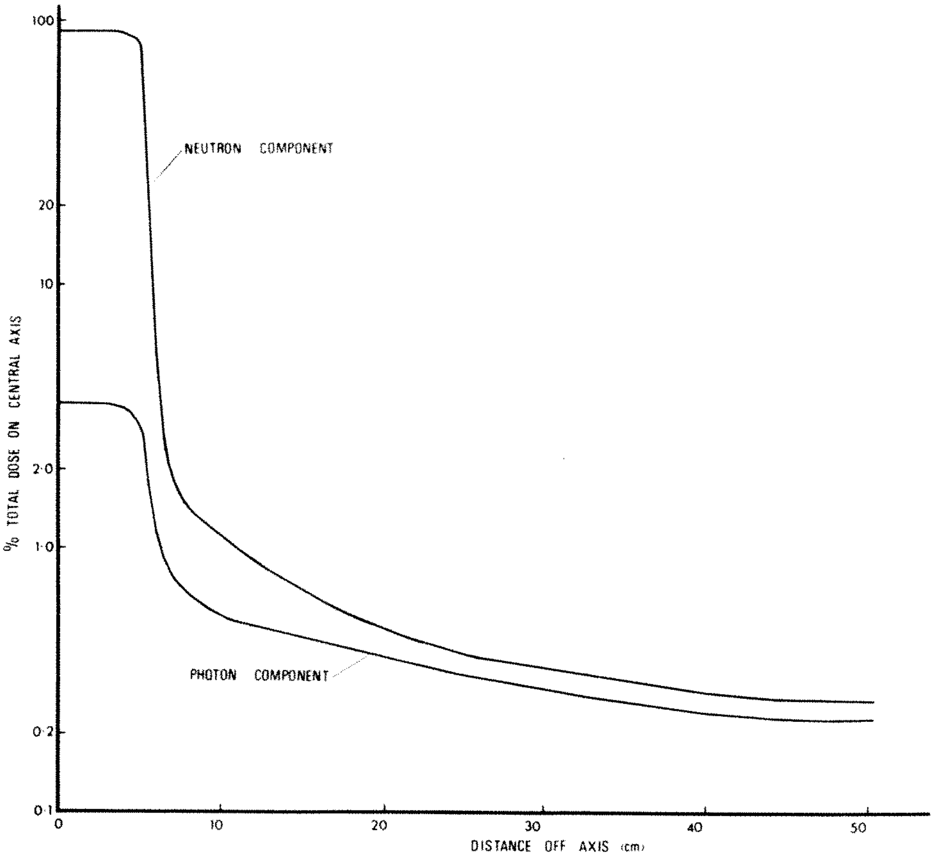

Fig. 4.
Neutron and γ ray profiles for 11 × 11 cm field at 125 cm FSD.

neutrons the sampling time has to be much greater. Sherwin (1974) discussed the statistical fluctuations in ionization chamber current which depend upon the quality of the primary radiation. He showed (Sherwin, 1976) that for ^{252}Cf neutrons the coefficient of variance of the ionization current was 16 times greater than for ^{60}Co γ rays. For the reasons previously stated the ionization chamber currents encountered in the neutron beam are typically a fifth of those for an X-ray beam. It can be shown that this increase in the coefficient of variance and the decrease in magnitude of the ionization current requires 80 times as many samples to be taken at each data point to achieve the same variance of the mean as found for the X-ray beam. In practice it was found that an increase in the number of samples by a factor of 30 was sufficient to achieve acceptable data, that is the time per sample was 6 s and the total time for each field condition was about 20 min. A similar time was required for the isodoses measured using the GM counter.

To correct for the lack of attenuation in the gas cavity of the ionization chamber the centre of measurement in the phantom was assumed to be three quarters of the radius of the cavity in front of the geometric centre of the chamber (Mijnheer *et al.* 1975).

Dose Distribution

Measurements in air

The effectiveness of the shielding cone and collimators at the treatment distance of 125 cm from the target was measured in air. Figure 3 shows a cross plot of an 11 × 11 cm collimator made using a tissue equivalent chamber. The measured 50% width was 10.8 cm and the penumbral width expressed as the distance between the 10% and 90% decrements was 0.9 cm. Outside the main beam the efficiency of the shielding was investigated using a ^{237}Np fission chamber and a GM counter to measure the neutron and γ components of the leakage radiation respectively. Measurements were made up to a distance of

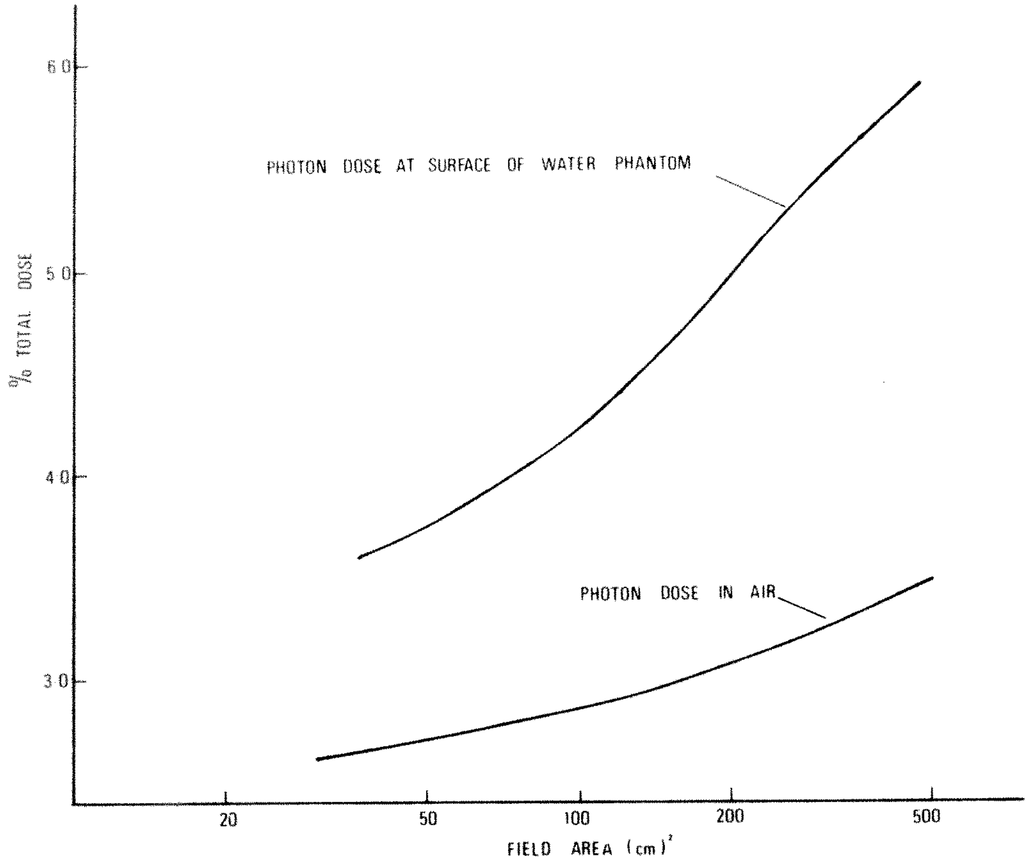

Fig. 5.

Variation of photon dose expressed as a percentage of total (neutron + γ) dose with field area.

50 cm perpendicular to the central axis and the results normalized to the total dose on the central axis are shown in Fig. 4. The neutron dose falls to 1% at a distance of 5.5 cm from the beam edge. At 50 cm from the central axis the neutron dose is 0.28% and the γ dose 0.22% of the total dose on the central axis, *i.e.* the photon contribution to the total dose is 44%.

At the standard treatment distance of 125 cm FSD the total dose-rate in air on the central axis was 0.445 rad min $^{-1}\mu$A^{-1} with a γ contribution of 3.0% for an 11 × 11 cm field. As stated previously, the maximum deuteron beam current is 100 μA. At present for radiotherapy a reduced beam current of 70 μA is used in order to reduce the power dissipation in the target and therefore to increase target life. This gives an approximate total dose-rate of 30 rad min^{-1}. The variation of γ contamination with equivalent square field area is shown in Fig. 5. To convert the area of a rectangular field to the equivalent square area it was assumed that the methods used in conventional photon therapy may be used for neutrons, that is that the side of the equivalent square field equals $2NM/(N+M)$ where N and M are the sides of the rectangular field. To test this relationship for neutrons the variation of the total dose per monitor unit in air with equivalent square field area was measured for field sizes in which there was a wide range in the ratio N:M. The results, given in Fig. 6, show that no significant error will be introduced by using the method of equivalent squares.

Parnell *et al.* (1972) calculated that the neutron dose-rate produced by deuterons on a thick beryllium target was 0.00027 $(E_d)^{2.7}$ rad min $^{-1}\mu$A^{-1} where E_d MeV is the energy of the deuteron beam and the dose-rate is measured at 125 cm FSD using a 5 × 5 cm field. For the 15 MeV deuteron beam the expected dose-rate is therefore 0.404 rad min$^{-1}\mu$A^{-1}. Using the data from Figs. 5 and 6 the measured total dose-rate for an 11 × 11 cm field can be converted to the neutron dose-rate for a 5 × 5 cm field,

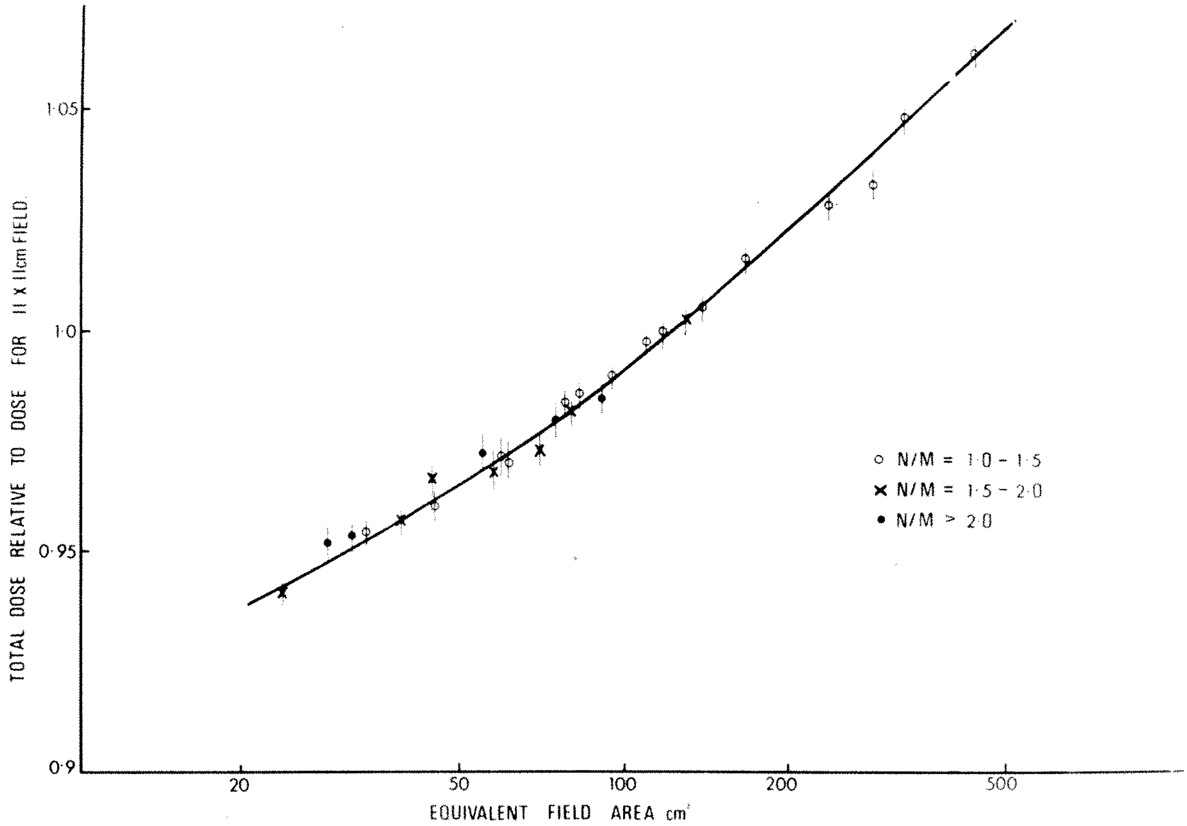

Fig. 6.

Variation of total dose-rate in air with equivalent field area at 125 cm FSD. Equivalent field area is calculated as $[2NM/(N+M)]^2$ where N and M are the sides of the rectangular field.

and the resulting dose-rate is 0.408 rad min $^{-1}\mu A^{-1}$, in excellent agreement with the predicted value.

Measurements in phantom

The dose build-up close to the surface was measured using a thin-window parallel-plate chamber and sheets of tissue equivalent (A-150) plastic and the maximum dose was found to occur at a depth of 1.5 mm with the 90% build-up occuring at a depth of 0.4 mm.

Depth-dose data for total dose and photon dose are shown in Tables III and IV. These data are based on the measurements at 15 field sizes between 4 × 7 cm and 21 × 21 cm at depth intervals of 1.8 cm. The data presented were interpolated from the measured data which were smoothed with depth and area. For clinical work photon doses are quoted as a percentage of the total dose at the surface of the phantom on the central axis. It is not possible to measure this directly since the depth of maximum build-up is small compared to the dimensions of the ionization chamber and the GM counter. To estimate the surface photon contamination, measurements of total and photon dose were made at a depth of 5 cm in the phantom. From these measurements the doses at the surface were calculated using the appropriate depth dose data, and the γ contamination was given by:

$$\Gamma(0,A) = \frac{\Delta_G(5,A)}{D_G(5,A)} \cdot \frac{D_T(5,A)}{\Delta_T(5,A)}$$

where $\Gamma(0,A)$ is the γ contamination at the surface of the phantom for a field of area A cm^2,

$\Delta_G(5,A)$; $\Delta_T(5,A)$ are the γ and total doses per monitor unit respectively at a depth of 5 cm on the central axis for a field of area A cm^2,

$D_G(5.A)$; $D_T(5,A)$ are the γ and total dose central axis percentage depth doses respectively at a depth of 5 cm for a field of area A cm^2.

However, the basic calibration of the monitor unit is

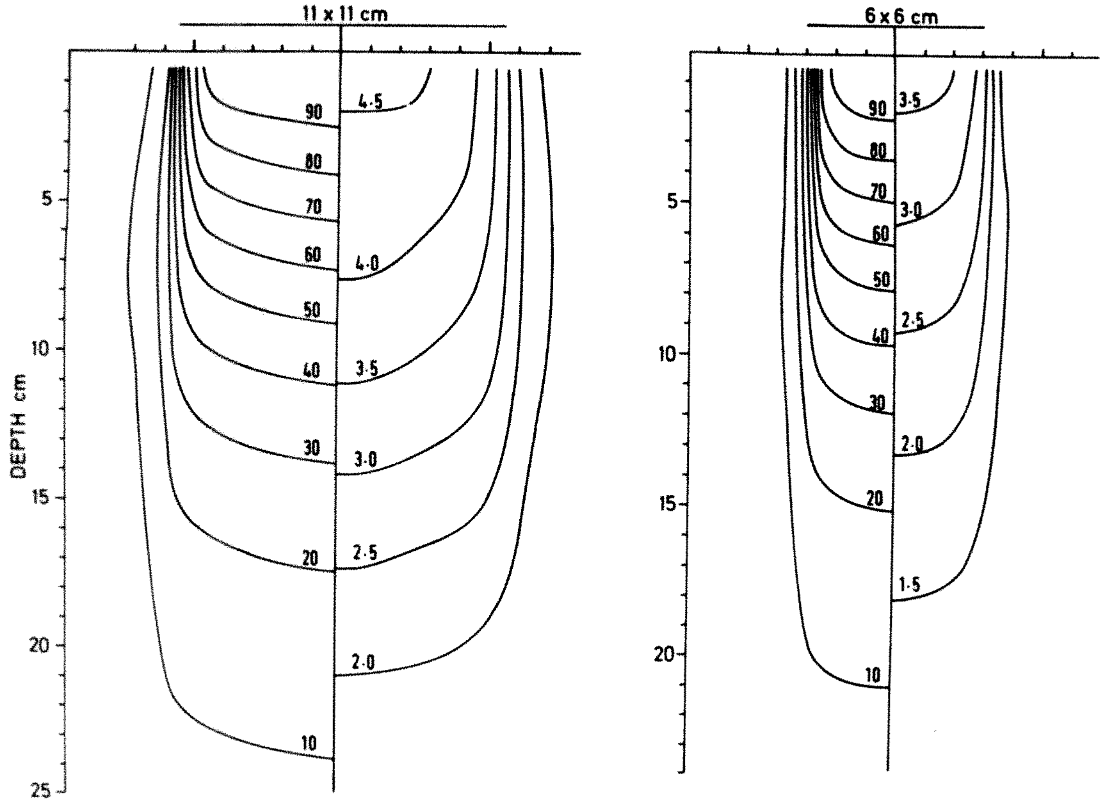

Fig. 7.

Isodose curves for 6 × 6 cm and 11 × 11 cm unwedged fields. (Left: neutron dose distribution; Right: photon dose distribution).

TABLE III

Percentage depth-dose data (neutron dose) at 125 cm FSD

Depth (cm)	Field size cm × cm 6 × 6	8 × 8	10 × 10	12 × 12	15 × 15	20 × 20
1	95.6	95.9	96.1	96.2	96.2	96.2
2	90.5	91.3	91.7	91.9	92.0	92.0
3	83.1	84.4	85.1	85.6	86.0	86.3
4	75.7	77.5	78.6	79.3	80.1	80.7
5	68.3	70.5	71.9	73.0	74.1	75.1
6	61.2	63.8	65.5	66.7	68.1	69.5
7	54.4	57.2	59.2	60.6	62.2	64.0
8	48.3	51.3	53.4	55.0	56.7	58.7
9	42.4	45.5	47.7	49.4	51.2	53.5
10	37.6	40.6	42.8	44.5	46.5	48.8
12	29.2	32.0	34.1	35.7	37.7	40.1
14	22.6	25.1	27.0	28.6	30.4	32.8
16	17.7	19.8	21.3	22.8	24.4	26.6
18	13.8	15.5	17.0	18.2	19.6	21.6
20	11.0	12.3	13.5	14.6	15.9	17.6

TABLE IV

Percentage depth-dose data (gamma dose) at 125 cm FSD

Depth (cm)	Field size cm × cm 6 × 6	8 × 8	10 × 10	12 × 12	15 × 15	20 × 20
1	96.7	97.7	98.4	99.2	100.3	101.9
2	93.5	95.3	96.9	98.4	100.4	103.6
3	90.3	92.9	95.2	97.3	100.2	104.4
4	87.0	90.3	93.3	96.0	99.6	104.8
5	83.5	87.5	91.1	94.3	98.5	104.6
6	79.9	84.6	88.6	92.2	96.9	103.7
7	76.2	81.5	86.0	90.0	95.0	102.4
8	72.6	78.3	83.1	87.2	92.6	100.3
9	69.0	75.0	80.1	84.4	90.1	98.1
10	65.4	71.6	76.8	81.2	86.9	95.2
12	58.5	64.6	69.8	74.3	80.2	88.6
14	52.1	57.6	62.6	66.9	72.8	81.1
16	46.3	51.1	55.6	59.6	65.1	73.3
18	41.0	45.2	49.3	52.9	57.7	65.1
20	36.4	40.0	43.6	46.7	51.0	57.7

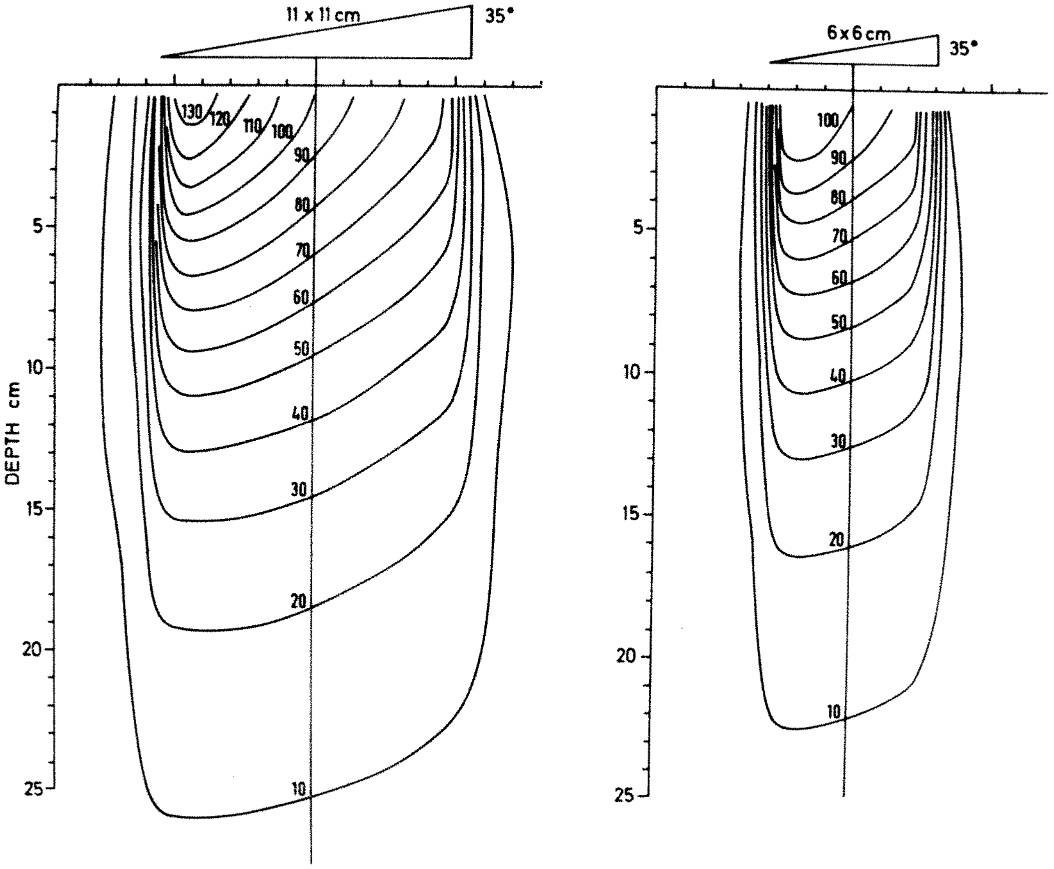

FIG. 8.
Isodose curves of neutron dose for 6 × 6 cm and 11 × 11 cm fields with 35 deg wedge.

made for an 11 × 11 cm field at a depth of 5 cm and, therefore, it is necessary to relate the gamma contamination at the surface to that measured for the calibration conditions. To do this two variables are defined, G (5,A) and T(5,A), which are the γ and total doses per monitor unit respectively at the reference depth normalized to the doses for an 11 × 11 cm field at that depth, viz:

$$G(5,\mathrm{A})=\frac{\Delta_{\mathrm{G}}(5,\mathrm{A})}{\Delta_{\mathrm{G}}(5,121)} \text{ and } T(5,\mathrm{A})=\frac{\Delta_{\mathrm{T}}(5,\mathrm{A})}{\Delta_{\mathrm{T}}(5,121)}$$

and therefore the γ contamination at the surface for a field of area A cm^2 is given by:

$$\Gamma(0,\mathrm{A})=\frac{G(5,\mathrm{A})}{T(5,\mathrm{A})}\cdot\frac{D_{\mathrm{T}}(5,\mathrm{A})}{D_{\mathrm{G}}(5,\mathrm{A})}\cdot\Gamma(5,121)$$

where $\Gamma(5,121)=\dfrac{\Delta_{\mathrm{G}}(5,121)}{\Delta_{\mathrm{T}}(5,121)}$

and is the γ contamination on the central axis for the calibration conditions.

Γ (0,A) is plotted against equivalent field area in Fig. 5.

A selection of isodose curves for plain and wedged field is shown in Figs. 7 and 8.

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REFERENCES

ATTIX, F. H., THEUS, R. B., and ROGERS, C. C., 1975. Measurements of dose components in an n–γ field. In *Proceedings of the Second Symposium on Neutron Dosimetry* *in Biology and Medicine, Neuherberg/München*, EUR 5273, Ed. G. Burger and H. G. Ebert, Vol.1, 329–340 (Commission of the European Communities, Luxembourg).

BEWLEY, D. K., 1970. Fast neutron beams for therapy. *Current Topics in Radiation Research*, *6*, 250–292.

BEWLEY, D. K., and PARNELL, C. J., 1969. The fast neutron beam from the MRC cyclotron. *British Journal of Radiology*, *42*, 281–288.

BOTTRILL, D. O., NIEMAN, M. J., and REDPATH, A. T., 1975. Rapid depth dose determination by a computer-controlled dosimetry system. *Physics in Medicine and Biology*, *20*, 980–989.

CATTERALL, M., 1974. The treatment of advanced cancer by fast neutrons from the Medical Research Council's cyclotron at Hammersmith Hospital, London. *European Journal of Cancer*, *10*, 343–347.

CATTERALL, M., SUTHERLAND, I., and BEWLEY, D. K., 1975. First results of a randomized clinical trial of fast neutrons compared with X or γ rays in treatment of advanced tumours of the head and neck. *British Medical Journal*, *2*, 653–656.

CATTERALL, M., BEWLEY, D. K., and SUTHERLAND, I., 1977. Second report on results of a randomized clinical trial of fast neutrons compared with X or γ rays in treatment of advanced tumours of the head and neck. *British Medical Journal*, *1*, 1642.

GREENE, D., and THOMAS, R. L., 1969. The attenuation of 14 MeV neutrons in steel and polyethylene. *Physics in Medicine and Biology*, *14*, 45–54.

HOUGH, J. H., 1977. Neutron sensitivity of a photon dosimeter. M.Sc. dissertation (University of Surrey).

INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, 1964. Physical Aspects of Irradiation, *N.B.S. Handbook 85* (Report 10b) (ICRU, Washington, D.C.).

1969. Radiation Dosimetry: X rays and γ rays with maximum photon energies between 0.6 and 50 MeV (Report 14) (ICRU, Washington, D. C.).

1977. Neutron dosimetry for biology and medicine (Report 26) (ICRU, Washington, D.C.).

MARUYAMA, T., and BOUTS, C. J., 1972. Attenuation of 15 MeV neutrons in multilayer shields composed of steel, polyethylene and borated materials. *Physics in Medicine and Biology*, *17*, 420–424.

MIJNHEER, B. J., BROERS-CHALLISS, J. E., and BROERSE, J. J., 1975. Measurements of radiation components in a phantom for a collimated *d–T* neutron beam. In *Proceedings of the Second Symposium on Neutron Dosimetry in Biology and Medicine, Neuherberg/München*, EUR 5273, Ed. G. Burger and H. G. Ebert, *1*, 423–443. (Commission of the European Communities, Luxembourg).

PARNELL, C. J., 1972. A fast neutron spectrometer and its use in determining the energy spectra of some cyclotron-produced fast neutron beams. *British Journal of Radiology*, *45*, 452–460.

PARNELL, C. J., OLIVER, G. D., ALMOND, P. R., and SMATHERS, J. B., 1972. The dose-rate of cyclotron-produced fast neutron beams. *Physics in Medicine and Biology*, *17*, 429–430.

SAUTTER, C. A., and ZIMMERMAN, E. J., 1965. Stopping cross sections of carbon and hydrocarbon solids for low-energy protons and helium ions. *Physical Review*, *140*, A490–A498.

SHERWIN, A. G., 1974. Developments in the use of ionization chambers for mixed field dosimetry. In *Proceedings of the Second Symposium on Neutron Dosimetry in Biology and Medicine, Neuherberg/München*, EUR 5273, Ed. G. Burger and H. G. Ebert, *1*, 341–358. (Commission of the European Communities, Luxembourg).

1976. Measurement of the dose components arising from Cf-252 by the method of stochastic current analysis. In *Basic Physical Data for Neutron Dosimetry*, EUR 5629, Ed. J. J. Broerse, 77–80 (Commission of the European Communities, Luxembourg).

SMATHERS, J. B., OTTE, V. A. SMITH, A., R., ALMOND, P. R., ATTIX, F. H., SPOKAS, J. J., QUAM, W. M., and GOODMAN, L. J., 1977. Composition of A-150 tissue equivalent plastic. *Medical Physics*, *4*, 74–77.

STORM, J. E., and ISRAEL, H. I., 1970. Photon cross-sections from 1 keV to 100 MeV for elements with $Z=1$ to $Z=100$. *Nuclear Data Tables*, *A7*, 565–681.

WAGNER, E. D., and HURST, G. S., 1961. A Geiger-Müller γ-ray dosimeter with low neutron sensitivity. *Health Physics*, *5*, 20–26.

WILLIAMS, J. R., LAW, J., BONNETT, D. E., and PARNELL, C. J., 1978. Initial experiences with the fast neutron facility at Edinburgh. In *Proceedings of the Third Symposium on Neutron Dosimetry in Biology and Medicine, Neuherberg/München.* EUR 5848, Ed. G. Burger and H. G. Ebert, 339–346. (Commission of the European Communities, Luxembourg).

WILLIAMSON, J., and WATT, D. E., 1972. The influence of molecular binding on the stopping power of the alpha particles in hydrocarbons. *Physics in Medicine and Biology*, *17*, 486–492.

Book review

Recent Advances in Ultrasound in Bio-Medicine, Volume 1 Editor D. N. White, pp. 256, Illust., 1977. (Research Studies Press, Oregon), $24.95.

My initial impression of this book was unfavourable since in the interest of speed it has been produced by the camera ready process, and a great deal of the content is written by and for physicists and engineers.

The book is intended to give the reader a fairly broad view of recent technical developments in the field of ultrasound equipment which may be expected to lead to ultrasound tissue characterization within the not too distant future. In addition to this, a number of other exciting developments including complex transducer design and acoustic holography have been included.

The first seven chapters give an exciting insight into a number of research projects concerning the interaction between ultrasonic waves and biological tissues. The limited clinical results included in some of these reports look extremely encouraging. The eighth chapter is a review of the type of image which can be obtained from current grey scale equipment. Unfortunately, the half tone images have not reproduced well but the chapter is nonetheless of value. Chapter nine is probably the weakest chapter in this book since it describes early results with one of the linear array scanners which by current standards must be regarded as rather primitive. The final chapter is a theoretical discussion of holography and I was disappointed to find that no clinical results or images have been included in this section.

The physician performing ultrasound examinations will probably not find this book digestible but those who are able to understand much of the physics within it will find this a very interesting, even exciting, addition to the literature.

H. B. MEIRE.

1979, *British Journal of Radiology*, *52*, 209–218 MARCH 1979

The response of six mouse tumours to combined heat and X rays: implications for therapy

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ABSTRACT

The response of six types of mouse tumour to single doses of X rays alone or to X rays in combination with moderate hyperthermia (42.5°C/60 min) has been assessed using delay in tumour regrowth. Thermal sensitization was observed in five of the six tumours. The degree of sensitization varied with the size of the X-ray dose, being larger at higher doses. The degree of sensitization also depended on the sequence and separation of the heat and irradiation.

The thermal sensitization has been measured in terms of the X-ray doses to produce the same level of tumour damage with or without heat, *i.e.* thermal enhancement ratios. These TER values, measured for X-ray doses in excess of 20 Gy, are not greater in any of the tumours than in a range of normal tissues, if the X rays and heat are given in close succession.

Separation of the heat and X rays reduces the TER values slightly, but some effect is still apparent at 3–24 hours. In normal tissues the effect of heat is totally lost within four hours. Comparison of these tumour data with published normal tissue data indicates a therapeutic advantage if the heat and X rays are separated by more than one hour. This therapeutic gain is most reliably achieved with heat given after irradiation.

Animal studies have shown that moderate hyperthermia when combined with radiation may be more effective than radiation alone in the palliation or control of malignant tumours (Crile, 1963; Overgaard and Overgaard, 1972; Robinson *et al.*, 1974; Yerushalmi and Har-Kedar, 1974; Thrall *et al.*, 1975). However, thermal sensitization to the effect of X rays is also observed in normal tissues (Robinson *et al.*, 1974; Thrall *et al.*, 1975; Field *et al.*, 1977; Stewart and Denekamp, 1977). Therefore in order to assess any clinical potential of a combined heat and X-ray treatment, the relative sensitivities of malignant and normal tissues must be compared.

Several normal tissue studies have demonstrated that thermal sensitization is greatest when heat is given simultaneously with, or immediately before or after the X rays, and gradually decreases as the interval between the two treatments increases (Stewart and Denekamp, 1977; Law *et al.*, 1977; Myers and Field, 1977; Hume and Field, 1978). In experimental tumours however, the picture is not quite so clear; when heat follows the X-ray dose, the thermal sensitization has been reported to decay more slowly (Stewart and Denekamp, 1978), or even to remain constant over a 48 hour interval (Overgaard, 1977).

The present study is an investigation of the thermal sensitization achieved in six types of mouse tumour with combined heat and X rays, and the effect of varying the sequence and interval between the two treatments. These data can be directly compared with those for mouse skin which were obtained under the same experimental conditions (Stewart and Denekamp, 1977) in order to assess the therapeutic gain and the possibility of an optimum treatment schedule.

MATERIALS AND METHODS

Six types of transplantable mouse tumour were studied, varying in tissue of origin, growth rate and degree of differentiation. All were of spontaneous origin in either WHT/Ht or CBA/Ht mice, and were maintained by subcutaneous implantation in the strain of origin.

The tumours were implanted under Penthrane anaesthesia, subcutaneously by trocar, on the ventral thorax of 8–12 week-old mice, except in the case of the anaplastic MT2 tumour which was implanted over the sacral region of the back. The tumours were monitored regularly until they reached a mean diameter of 5–6.5 mm, at which time they were selected for treatment and randomly allocated to X rays alone or combined heat and X rays.

The mice were anaesthetized with 60 mg/kg sodium pentobarbitone 10 min before irradiation and/or heating in a precision controlled, circulating water bath (accuracy ±0.05°C), at a temperature of 42.8°C. During heating, the mice were lightly taped into lead and Perspex irradiation jigs, and suspended on the surface of the water with the tumour immersed. The temperatures of sample tumours were monitored with a 29 gauge thermocouple probe and found to stabilize at 0.2–0.3°C lower than the water bath temperature, within 5–15 min of immersion. Variations in temperature across the tumour volume were not more than 0.1°C. These sample tumours were not included in the experiments. Heating was always for a period of 60 min and was applied at intervals between 0 and 24 hours before or after the X-ray dose.

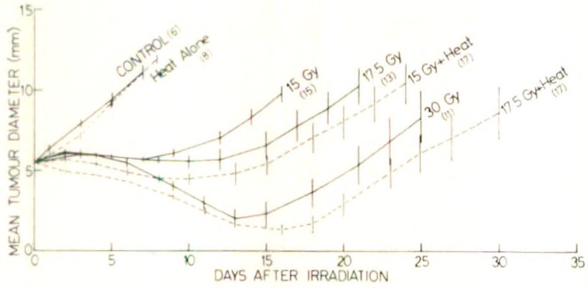

Fig. 1.

Growth curves for untreated and treated tumours (squamous carcinoma D). Each curve represents the mean of a group of animals (number shown in brackets) with the vertical bars representing ±1 standard error of the mean. Solid lines are for X rays alone. Dashed lines are for X rays followed immediately by one hour at 42.5°C.

Irradiations were performed using 240 kV X rays at a dose-rate of 2.4 Gy/min (0.25 mm Cu+1 mm Al filter; HVL 1.3 mm Cu). Four mice were irradiated simultaneously and turned through 180 deg. halfway through the irradiation, to ensure uniform dose throughout the tumour mass. Groups of 5 to 17 animals were treated at each dose over a range of X-ray doses, with or without added heat.

After treatment, the squamous carcinomas D, Ca NT′ and the sarcomas F and MT2 were measured three times per week using vernier callipers over three perpendicular diameters until they reached 12 mm average diameter, at which time the mice were sacrificed. The two slower-growing tumours, the slow sarcoma S and the slow Rh carcinoma (volume doubling time more than six days) were

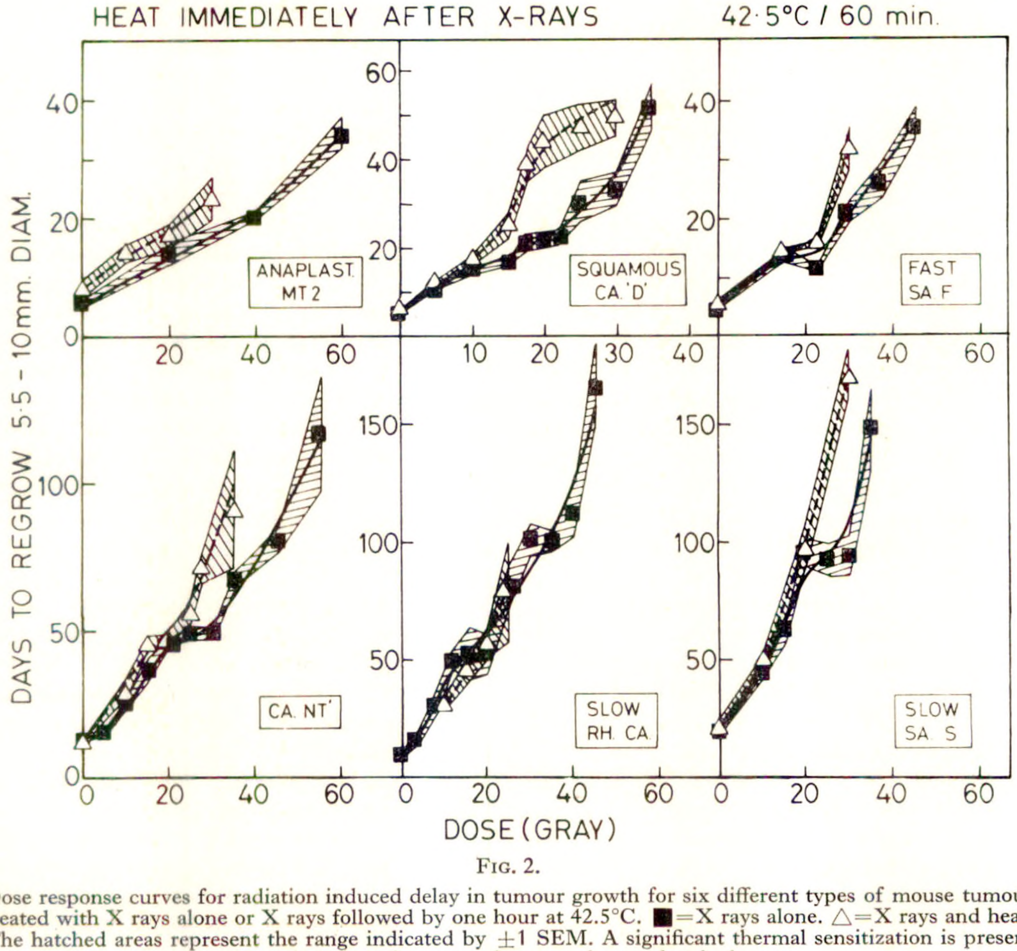

Fig. 2.

Dose response curves for radiation induced delay in tumour growth for six different types of mouse tumour treated with X rays alone or X rays followed by one hour at 42.5°C. ■=X rays alone. △=X rays and heat. The hatched areas represent the range indicated by ±1 SEM. A significant thermal sensitization is present where there is a clear space between the two hatched areas.

measured weekly. The number of days taken to grow to a size 4.5 mm larger than the size at irradiation (*i.e.* 5.5 to 10 mm mean diameter, equivalent to 2.5 volume doublings) was calculated for each tumour. From these individual regrowth times a mean regrowth time and standard error of the mean could be calculated for each dose group, and plotted against the dose of X rays.

RESULTS

Figure 1 shows a series of growth curves for the squamous carcinoma D treated with single doses of X rays, or with X rays followed immediately by one hour's heat. Growth curves for animals which received no treatment or one hour's exposure to heat alone (42.5°C) were not significantly different. Tumours irradiated with increasing X-ray doses showed an increasing delay in regrowth. When the heat and X-ray doses were combined, longer regrowth delay was seen than with X rays alone, indicating significant thermal sensitization. To construct dose response curves the time for each tumour to grow from a treatment size of 5.5 mm to 10 mm mean diameter (or equivalent) was estimated and the mean delay for each treatment group was plotted against X-ray dose.

Figure 2 shows the dose response curves for all six tumours treated with X rays alone or with X rays followed immediately by one hour's heat. The area contained by the error bars on each point has been hatched to make it easier to determine when there is a definite separation of the two sets of data; a white space between the lines indicates that there is a significant thermal enhancement. In each tumour there is little or no sensitization at low X-ray doses, but at higher doses the curve for X rays alone breaks towards a more resistant response, whereas the curve for heated tumours does not. The "break-point" is

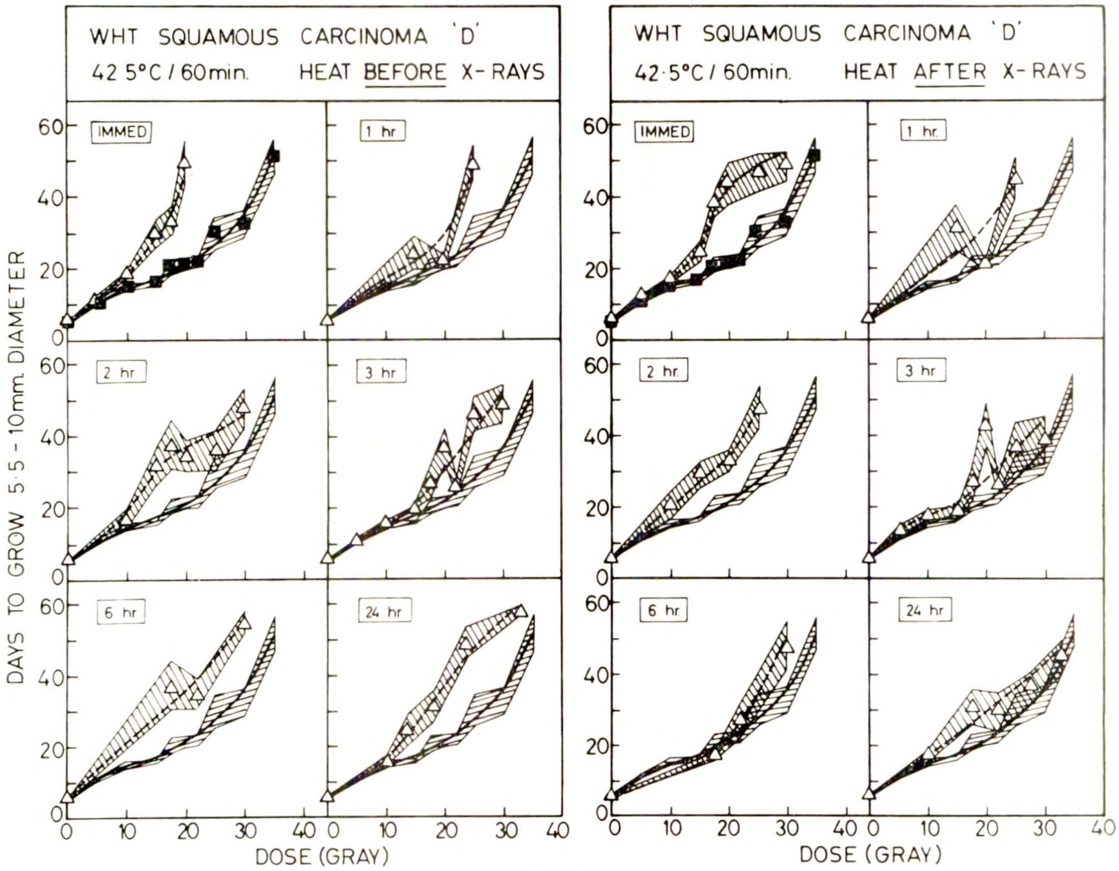

FIG. 3

Dose response curves for squamous carcinoma D treated with X rays alone (■) or with X rays and heat (△) applied at the stated intervals before or after irradiation. The hatched area represents the range from ±1 SEM. The points for X rays alone (■) are only shown in the first of each set of panels; thereafter the hatched area is reproduced without points.

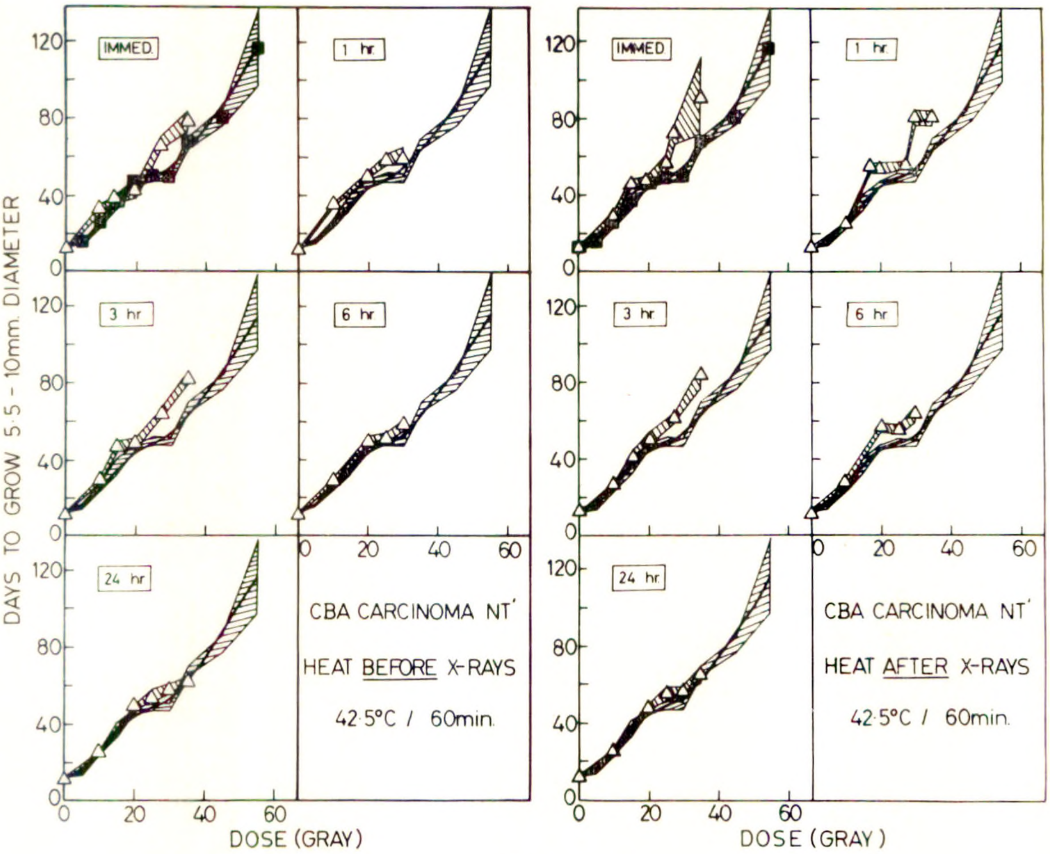

Fig. 4.

Dose response curves for the mammary carcinoma NT′, treated with X rays alone or with X rays and heat applied at the stated intervals before or after irradiation ■=X rays alone. △=X rays plus heat (42.5°C/1 hour).

believed to represent the transition from well oxygenated to hypoxic response (Thomlinson and Craddock, 1967). At higher doses four of the tumours (squamous carcinoma D, fast sarcoma F, slow sarcoma S and the mammary carcinoma NT′) show a definite separation of the two hatched areas, indicating a significant thermal enhancement. The anaplastic MT2 tumour does not show a significant sensitization by heat, although the heat-treated groups all showed a longer delay than those treated with X rays alone. In this tumour heat alone caused some growth delay, unlike the other tumours. Only one of the tumours tested, the slow Rh carcinoma, showed no thermal enhancement at any of the dose levels tested, but it is possible that these studies did not extend to a high enough X-ray dose.

The thermal enhancement ratios (TER) which can be measured from these curves are very dependent on the dose level at which they are calculated. TER's ranging from about 1.0 (slow Rh carcinoma) to about 1.6 (squamous Ca D and MT2 tumours) can be measured above an X-ray dose of 20 Gy on the control curves.

Figures 3 and 4 show the response of the squamous carcinoma D and the carcinoma NT′ to a constant heat dose of 42.5°C for 60 min, applied at various intervals before or after irradiation. In the squamous carcinoma D (Fig.3), when heat was applied before irradiation, there was significant thermal sensitization at each of the time intervals tested as evidenced by the clear separation of the two hatched areas; however, there is scatter on the data and the errors are large, making it difficult to measure accurate thermal enhancement ratios. The large errors are mainly due to the presence of locally controlled tumours in many of the heat-treated groups; such tumours were included in the analysis as 60 days delay, as this is the latest time at which a recurrent tumour has been observed. Heat-treated tumours fell into two categories, even in the same batch of mice; tumours which responded only slightly better than those treated with X rays alone and tumours on which the treatment was very effective.

When heat was applied after irradiation to Sq Ca D the data are again scattered and show large errors. Only when the heat dose was applied immediately after, or at an interval of two hours after irradiation, was there a significant thermal enhancement at all dose levels above the "break-point" at 10 Gy; at all other intervals the data are ambiguous, suggesting an enhancement at some dose levels but not at others.

The other tumour which we have studied extensively is the mammary carcinoma NT′, and Fig. 4 shows the regrowth data for this tumour at each of the intervals tested. For Ca NT′, when heat was applied before irradiation there was a significant thermal sensitization only when the heat immediately preceded the irradiation or when there was a gap of three hours between the two treatments. There was little or no effect at the other time intervals. When the heat was given after irradiation, however, the sensitization remained longer, with some thermal enhancement present at six hours, although this had virtually disappeared by 24 hours.

Similar dose response curves were drawn for the other four tumours at all the time intervals tested, enabling thermal enhancement ratios to be measured at any level of damage. These values, measured above an X-ray dose of 20 Gy, are summarized in Table I together with some details of the tumour characteristics.

DISCUSSION

Consecutive heat and irradiation

The present results indicate that for single dose treatments a significant thermal sensitization of tumours to X rays can be produced by 60 min immersion in hot water, with an intra-tumour temperature of 42.5°C. Five of the six tumours tested showed considerable sensitization when heat was applied immediately after irradiation. In the sixth, the slowly growing Rh carcinoma, no effect was seen with the X-ray doses used (up to 20 Gy), but we cannot exclude the possibility that thermal sensitization would have been seen at higher doses. In most of the tumours there was clearly a greater degree of sensitization at higher X-ray doses, corresponding to the region where the response to X rays is dominated by the radioresistant hypoxic cells. These cells may be more thermosensitive as a result of their hypoxia (*e.g.* Kim *et al.*, 1975; Gerweck, 1977; Dewey *et al.*, 1977), or as a result of the nutritional deficiency (Hahn, 1974), reduced pH (Overgaard and Overgaard, 1975; Gerweck and Rottinger, 1976) or the accumulation of metabolites that will also occur at a

TABLE I

Tumour	Time interval (hours)	TER		Volume doubling time, 6.5–8.2 mm	Therapeutic gain relative to skin	
		Heat after X	Heat before X		Heat after X	Heat before X
Squamous carcinoma D	0	1.5–1.7	1.6–1.8	2 days	0.8–0.9	0.9–1.0
	1	1.2–1.3	1.2–1.3		0.9–1.0	0.8–0.9
	2	1.4–1.8	1.5–1.9		1.1–1.5	1.1–1.4
	3	1.2–1.3	1.3–1.4		1.1–1.2	1.1–1.2
	6	1.0–1.2	1.4–1.5		1.0–1.2	1.2
	24	1.0–1.4	1.2–1.4		—	—
Carcinoma NT′	0	1.2–1.4	1.1–1.3	4.5 days	0.7–0.8	0.6–0.8
	1	1.3–1.5	1.2–1.4		1.0–1.2	0.9–1.0
	3	1.2–1.4	1.2–1.3		1.1–1.3	1.0–1.1
	6	1.2–1.5	1.2–1.3		1.2–1.5	1.0–1.1
	24	1.1–1.3	1.1–1.3		—	—
Slow sarcoma S	0	1.1–1.3	—	7.5 days	0.6–0.7	—
	1	1.2–1.4	—		0.1–1.1	—
	3	1.0–1.1	—		0.9–1.0	—
	6	1.0–1.1	—		1.0–1.1	—
Fast sarcoma F	0	1.2–1.4	—	1.8 days	0.7–0.8	—
	3	1.2–1.3	—		1.1–1.2	
MT2	0	1.5–1.7	—	2 days	0.8–0.9	—
Slow RH carcinoma	0	1.0	—	9 days	0.5	—

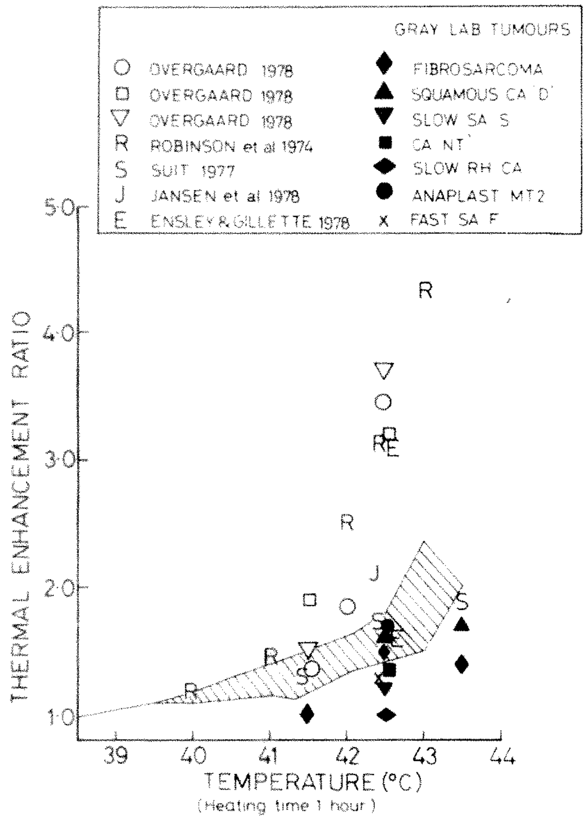

Fig. 5.

Thermal enhancement ratios calculated from pairs of dose-response curves obtained with X rays alone or in combination with heat. Published data for tumours heated for one hour during or shortly before or after irradiation are shown by open symbols; the authors are identified in the key. The closed symbols represent the six tumours presented in this paper and the fibrosarcoma data of Stewart and Denekamp (1977). The hatched area represents the range of normal tissue data (Robinson *et al.*, 1974; Stewart and Denekamp, 1977; Law *et al.*, 1977; Myers and Field, 1977; Jansen *et al.*, 1978; Hume and Field, 1978; Ensley and Gillette, 1979). All of our tumour data fall within or below the range of TER values for normal tissues, indicating no therapeutic gain.

distance from the capillaries. The fact that only a small effect is observed at low radiation doses would imply that the radiation sensitivity of the heat-sensitized hypoxic cells is still less than that of the normally oxygenated cells that dominate the response at low doses. Similar observations of the dependence of TER on X-ray dose have been made for other tumours (Yerushalmi, 1976; Stewart and Denekamp, 1978) and also for normal tissues (Myers and Field, 1977; Field and Law, 1978), although in one of the normal tissue studies fractionated treatments were used and the reduced TER values may be reflecting induced thermal tolerance. If the dose per fraction is important in fractionated treatments, it is possible that a smaller thermal enhancement ratio will be seen than with large single doses.

Two of the tumours (Sq Ca D and Ca NT′) have been tested with heat immediately before irradiation and a similar degree of thermal sensitization was observed (Table I). A quantitative measure of the thermal sensitization can be derived from the curves in Fig. 2, by taking the ratio of doses to produce the same effect (TER). These values have been estimated for each tumour at doses above 20 Gy and are plotted in Fig. 5 together with data from the literature for other tumours and for normal tissues. The hatched area represents the range of values for normal tissues (mouse skin and intestine and cartilage of baby rats). The closed symbols represent the seven tumours studied at the Gray Laboratory and all treated under identical conditions. These include the six tumours presented here and a fibrosarcoma (Stewart and Denekamp, 1978).

The relative position of the TER values for tumour and normal tissue is an indication of whether there is likely to be any benefit from using heat and X rays rather than X rays alone. The results from Overgaard on three different tumours lie well above the normal tissue data, indicating a therapeutic gain with hyperthermia. However, these tumours were treated with 27 MHz short wave diathermy so the temperature distribution is likely to have been very heterogeneous, and the precise temperature is difficult to measure (Overgaard, personal communication). The C_3H mammary tumour data of Robinson *et al.* (1974) in which there may have been some compromise of the vasculature, and one set of data from Ensley and Gillette (1979) also lie significantly above the normal tissue data. All of our data, and many of those from the literature, fall within or even below the thermal enhancement ratios observed in normal tissues, indicating no general therapeutic advantage of heat plus X rays relative to X rays alone, when there is no interval of time between the two treatments.

Ensley and Gillette (1979) using the C_3H mammary adenocarcinoma demonstrated an advantage of combined heat and irradiation only when the two were given simultaneously (TER=3.1), with a loss of thermal sensitization when the heat immediately followed irradiation (TER=1.6). This, together with the data of Robinson *et al.* (1974), also for the C_3H mammary tumour, irradiated in the middle of the heating period, suggests that the *exact* coincidence of heat and irradiation may be very important. This is supported by the *in vitro* data of Joshi *et al.* (1976), Meyer *et al.* (1977) and Sapareto *et al.* (1978).

However, Hirst *et al.* (1978) and Overgaard (1977), using experimental tumours, have shown no significant difference for concurrent or consecutive heat and X rays.

It is clear from Fig. 5 that no universal advantage of combined heat and X rays in close succession has been demonstrated. In our own experiments none of the tumours showed a therapeutic gain. The only occasion when a very high thermal sensitization has been observed in our tumours, for heat and radiation given closely together, was when a metal clamp had been used to occlude the blood supply (Hill and Denekamp, 1978) or when the tumour had been grown in a very constricted site, subcutaneously on the tail (unpublished data).

Varying the interval

The thermal sensitization to X rays has been shown to fade if an interval of time elapses between the two treatments, both *in vitro* (Kim *et al.*, 1974; Kal *et al.*, 1975; Li *et al.*, 1976; Harris *et al.*, 1977) and for normal tissues *in vivo* (Stewart and Denekamp, 1977; Law *et al.*, 1977; Myers and Field, 1977; Hume and Field, 1978) and for tumours in mice (Crile, 1963; Thrall *et al.*, 1975; Alfieri *et al.*, 1975; Jansen *et al.*, 1978; Stewart and Denekamp, 1978).

In the present experiments separation of the heat and irradiation was also shown to reduce the TER in Sq Ca D, although possibly not in Ca NT′ (Figs. 3 and 4 and Table I). It has previously been suggested that this loss of TER may be slower (Stewart and Denekamp, 1978) or less complete (Jansen *et al.*, 1978) in tumours than in normal tissues; Overgaard (1977) found *no* loss of sensitization with intervals of up to 48 h. Thus it appears that a therapeutic advantage might be gained from heat and X rays if the two modalities are given at an appropriate spacing. For a variety of normal tissues the TER falls to unity if the heat is applied four hours after X rays (Hume and Field, 1978). A similar but very much less predictable and slower decline of TER is observed if heat is given first. Thus if heat is applied three to four hours after irradiation no thermal sensitization of normal tissues occurs, and there is no necessity to reduce the radiation dose in order to remain within the tolerance of the normal tissues. The TER values at different times in the four tumours are summarized in Table I; an advantage is seen in three of the four tumours when heat is applied at three hours after irradiation.

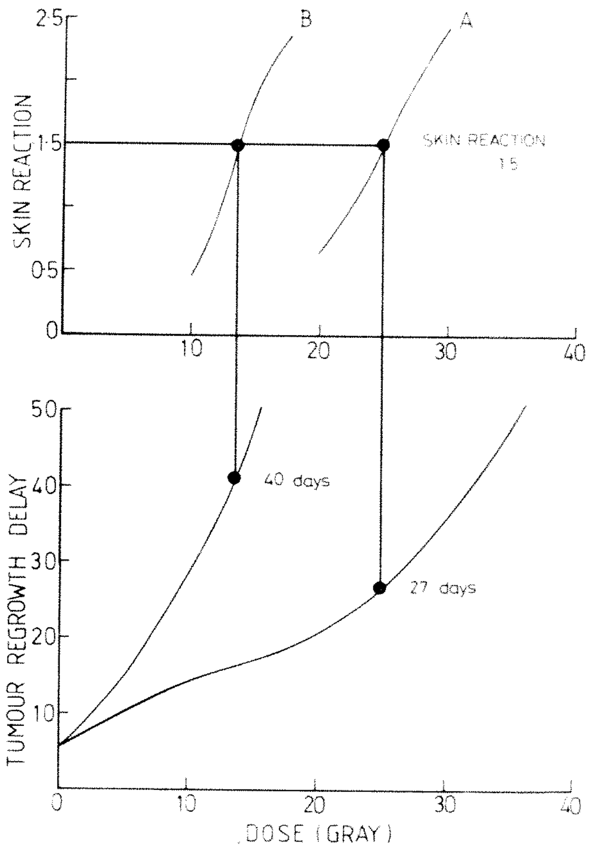

Fig. 6.

Schematic diagram to demonstrate the method of comparing the effectiveness of two treatments, A and B, by standardizing to a constant level of normal tissue injury. For a skin reaction of 1.5 treatment B gives more tumour growth delay (40 days) than treatment A (27 days). This analysis is only possible if comparable treatments have been used on the tumour and the normal tissue.

Since TER values vary with the X-ray dose used, it is important to compare tumour and normal tissue TER's obtained over the same dose range. Higher values may be obtained in tumours if the endpoint used requires high X-ray doses, *e.g.* TCD50 assays. A more appropriate way of demonstrating the therapeutic gain is shown schematically in Fig. 6. Two sets of normal tissue and tumour data obtained for different treatments have been compared in terms of the tumour damage which may be achieved for a constant level of normal tissue damage. In Fig. 6 the doses to produce an average skin reaction level of 1.5, equivalent to moderate moist desquamation with complete healing (Denekamp, 1975), can be derived, and then the tumour delay produced by these doses in treatments A and B can be compared from the lower curves. In the example shown, treatment B is more effective (40 days delay) than treatment A (27 days delay) for the same skin reaction.

This approach has been used with the published skin reaction data of Stewart and Denekamp (1977) used as the normal tissue control. The results were obtained in almost the same experimental arrangement as that used for the present tumour experiments. Figure 7 shows this analysis for four of the tumours; tumour growth delay for a skin reaction of 1.5 is plotted against the interval between irradiation and heating. In each diagram, the horizontal dashed line corresponds to the growth delay produced by X rays alone and the shaded band indicates the error on this value (±1 sem). When a treatment produces increased tumour damage relative to the skin, *i.e.* a therapeutic gain, the data points fall above the shaded area.

For each of these tumours, these curves demonstrate that a thermal treatment applied immediately before or after irradiation is in fact worse than treating with X rays alone; the points all fall within or below the shaded area. Separation of the two treatments however results in a more beneficial response. In the carcinoma NT′ and the fast Sa F there is a distinct advantage when the heat dose is applied three hours after irradiation, an effect which persists at least to six hours in the carcinoma NT′. This therapeutic advantage when heat follows irradiation is not so clear in the other two tumours, where the errors overlap, but it is still apparent that an interval of a few hours between the two modalities is better than consecutive treatment.

No conclusions can be drawn from the data for the two tumours heated before irradiation. Again, an interval of a few hours produces a therapeutically better response than heat and X rays in close succession. In the carcinoma NT′ the points still fall within the control range, indicating that heat applied after irradiation would be the treatment of choice, as suggested by Stewart and Denekamp (1978), while

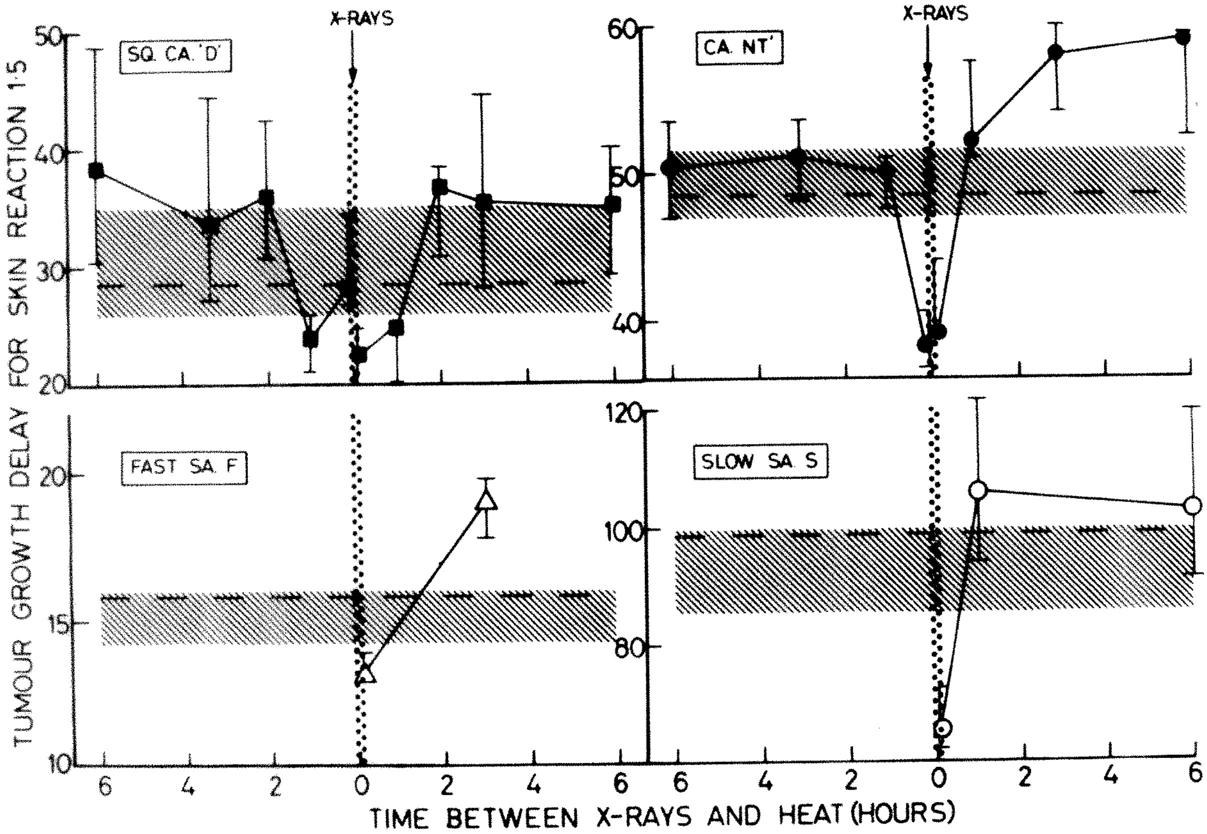

Fig. 7.

Effect on four tumours for a constant level of normal tissue damage, as a function of the time between heating and irradiation. The hatched area represents the delay achieved with X rays alone ±1 sem. Heat and irradiation given in close sequence are worse than X rays alone. If an interval longer than one hour elapses between the two treatments the combined heat and irradiation is better than X rays alone, *i.e.* shows a therapeutic gain.

the situation seen for squamous carcinoma D suggests no difference due to sequence of application. However, for heat before irradiation the X-ray dose must be reduced to avoid exceeding the normal tissue tolerance.

The trends and conclusions suggested by these diagrams remain the same whether the data are analysed using a skin reaction of 1.0 (severe reddening and/or swelling) or 2.0 (breakdown of most of the skin) instead of the 1.5 level chosen here.

Overgaard (1978) and Jansen *et al.* (1978) have suggested that two separate effects may be combined in the response of tumour cells to heat and X rays. These are direct thermal killing and true radiosensitization. If the two treatments are separated in time the direct cell killing effect would persist but the interaction of X rays and heat would fade. Since the thermal sensitization disappears completely for normal tissues with an interval of a few hours, it is postulated that in normal tissues there is no direct component of thermal killing. Thus any advantage obtained by an appropriate separation of the X rays and heat would result from the additive effects of X-ray killing and heat killing in the tumour, and no increased effect relative to X rays alone in the normal tissues. The combination of X rays and heat would then be better than either alone because the population that is resistant to X rays has a high sensitivity to heat.

From our own results it is difficult to separate the response of the tumours into direct heat damage and thermal radiosensitization. Only one tumour (MT2) showed an effect of heat alone, but if the heat sensitive population represents only a small proportion of the total cells, it would be difficult to detect it with heat alone. The greater thermal enhancement ratios at higher X-ray doses indicate a bigger effect of heat on the cells which are normally radioresistant, *i.e.* those most distant from the blood vessels. Thermal sensitization persists beyond three hours in the two tumours tested, with a small effect even at 24 hours. This could be interpreted as support for the concept of direct thermal killing, and would agree with the data of Jansen *et al.* (1978) and Overgaard (1978). However, the results of Alfieri *et al.* (1975), Thrall *et al.* (1975), and Stewart and Denekamp (in preparation), which show that the thermal interaction is totally lost by 24 hours, would not support the concept of direct thermal killing. This is clearly an area requiring further study.

Conclusions

1. Sensitization of tumours to X irradiation was achieved in five out of six tumour types using water-bath heating to give an intra-tumour temperature of 42.5°C.
2. The extent of thermal sensitization was dependent on the size of X-ray dose used, being larger at high X-ray doses.
3. The thermal sensitization of the tumours was no greater than that in normal tissues if the heat was given shortly before or after irradiation.
4. A slight loss of sensitization was observed if the two treatments were separated in time but sensitization was still apparent at three to twenty-four hours.
5. A therapeutic advantage, relative to skin damage, was only observed if the heat and X rays were separated by more than one hour. The most reliable single-dose treatment would be with heat after irradiation.

Acknowledgments

We should like to thank Mr. P. W. Sheldon for assistance in part of this work; Mrs. Lynda Hall and her staff for care of the animals, Dr. H. B. Hewitt for providing the tumours and Prof. J. F. Fowler, Dr. S. B. Field and Miss F. A. Stewart for their helpful criticisms and discussions. We are grateful to the Cancer Research Campaign for their financial support.

REFERENCES

Alfieri, A. A., Hahn, E. W., and Kim, J. H., 1975. The relationship between the time of fractionated and single doses of radiation and hyperthermia on the sensitization of an *in vivo* mouse tumour. *Cancer*, *36*, 893–903.

Crile, G., 1963. The effects of heat and radiation on cancers implanted on the feet of mice. *Cancer Research*, *23*, 372–380.

Denekamp, J., 1975. Residual radiation damage in mouse skin 5 to 8 months after irradiation. *Radiology*, *115*, 191–195.

Dewey, W. C., Thrall, D. E., and Gillette, E. L., 1977. Hyperthermia and radiation—a selective thermal effect on chronically hypoxic tumour cells *in vivo*. *International Journal of Radiation Oncology, Biology and Physics*, *2*, 99–103.

Ensley, B. A., and Gillette, E. L., 1979. Effect of heating order on radiation response of mouse tumour and skin. *International Journal of Radiation Oncology, Biology and Physics*, (in press).

Field, S. B., Hume, S. P., Law, M. P., and Myers, R., 1977. The response of tissues to combined hyperthermia and X rays. *British Journal of Radiology*, *50*, 129–134.

Field, S. B., and Law, M. P., 1978. The response of skin to fractionated heat and X rays. *British Journal of Radiology*, *51*, 221–222.

Gerweck, L. E., 1977. The lethal response of cells to radiation or hyperthermia under acute and chronic hypoxic conditions (Abstract). *Radiation Research*, *70*, 612.

Gerweck, L. E., and Rottinger, E., 1976. Enhancement of mammalian cell sensitivity to hyperthermia by pH alteration. *Radiation Research*, *67*, 508–511.

Hahn, G. M., 1974. Metabolic aspects of the role of hyperthermia in mammalian cell inactivation and their possible relevance to cancer treatment. *Cancer Research*, *34*, 3117–3123.

Harris, J. R., Murthy, A. K., and Belli, J. A., 1977. The effect of delay between heat and X irradiation on the survival response of plateau phase V-79 cells. *International Journal of Radiation Oncology, Biology and Physics*, *2*, 515–519.

Hill, S. A., and Denekamp, J., 1978. The effect of vascular occlusion on the thermal sensitization of a mouse tumour. *British Journal of Radiology 51*, 997-1002.

Hirst, D. G., McNally, N. J., George, K. C., and Chu, A. M., 1978. The interaction of heat and radiation in a mouse sarcoma. Proceedings of 2nd International Symposium on Cancer Therapy by Hyperthermia and Radiation, June 2–4, 1977, Essen, Germany. Eds. Streffer *et al.* (Urban and Schwarzenberg, Munich) p. 253–254.

Hume, S. P., and Field, S. B., 1978. Hyperthermic sensitization of mouse intestine to damage by X rays: the effect of sequence and temporal separation of the two treatments. *British Journal of Radiology, 51*, 302–307.

Jansen, W., Van Der Schueren, E., and Breur, K., 1978. Thermal enhancement of the radiation response of the skin and a mammary carcinoma in mice. Proceedings of 2nd International Symposium on Cancer Therapy by Hyperthermia and Radiation, June 2–4, 1977, Essen, Germany. Eds. Streffer *et al.*, (Urban and Schwarzenberg, Munich) p. 253–254.

Joshi, D. S., Van Der Schueren, E., Deys, B. F., and Barendsen, G. W., 1976. Factors influencing the interaction between hyperthermia and ionizing radiation with respect to mammalian cell reproductive death (Abstract). *International Journal of Radiation Biology, 29*, 184.

Kal, H. B., Janse, H. C., and Gaiser, F. J., 1975. Repair of radiation and hyperthermia induced lesions in rat rhabdomyosarcoma cells *in vitro*. Annual report of Radiobiology Institute, Rijswijk, The Netherlands.

Kim, J. H., Kim, S. H., and Hahn, E., 1974. Thermal enhancement of the radiosensitivity using cultured normal and neoplastic cells. *The American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 121*, 860–864.

Kim, S. H., Kim, J. H., and Hahn, E. W., 1975. Enhanced killing of hypoxic tumour cells by hyperthermia. *British Journal of Radiology, 48*, 872–874.

Law, M. P., Ahier, R. G., and Field, S. B., 1977. The response of mouse skin to combined hyperthermia and X rays. *International Journal of Radiation Biology, 32*, 153–163.

Li, G. C., Evans, R. G., and Hahn, G. M., 1976. Modification and inhibition of repair of potentially lethal X-ray damage by hyperthermia. *Radiation Research, 67*, 491–501.

Meyer, K. R., Gillette, E. L., and Hopwood, L., 1977. Effect of heating and irradiating order on MADCAP 37 tumour cells (Abstract). *Radiation Research, 70*, 630.

Myers, R., and Field, S. B., 1977. The response of the rat tail to combined heat and X rays. *British Journal of Radiology, 50*, 581–586.

Overgaard, J., 1977. The effect of sequence and time intervals of combined hyperthermia and radiation treatment of a solid mouse mammary adenocarcinoma *in vivo*. *British Journal of Radiology, 50*, 763–764.

1978. The effect of local hyperthermia alone and in combination with radiation on solid tumours. Proceedings of 2nd International Symposium on Cancer Therapy by Hyperthermia and Radiation, June 2–4, 1977, Essen, Germany. Eds. Streffer *et al.*, (Urban and Schwarzenberg, Munich) p. 49–61.

Overgaard, J., and Overgaard, K., 1975. Effect of environmental acidity on the hyperthermic treatment of tumour cells. *IRCS Medical Science: Biochemistry; Cancer; Cell and Membrane Biology, 3*, 386.

Overgaard, K., and Overgaard, J., 1972. Investigations on the possibility of a thermic tumour therapy—II. Action of combined heat-roentgen treatment on a transplanted mouse mammary carcinoma. *European Journal of Cancer, 8*, 573–575.

Robinson, J. E., Wizenberg, M. J., and McCready, W. A., 1974. Radiation and hyperthermal response of normal tissue *in situ*. *Radiology, 113*, 195–198.

Sapareto, S. A., Hopwood, L. E., and Dewey, W. C., 1978. Combined effects of X-irradiation and hyperthermia on CHO cells for various temperatures and orders of application. *Radiation Research, 73*, 221–233.

Stewart, F. A., and Denekamp, J., 1977. Sensitization of mouse skin to X-irradiation by moderate heating. *Radiology, 123*, 195–200.

1978. The therapeutic advantage of combined heat and X rays on a mouse fibrosarcoma. *British Journal of Radiology, 51*, 307–316.

Suit, H. D., 1977. Hyperthermic effects on animal tissues. *Radiology, 123*, 483–487.

Thomlinson, R. H., and Craddock, R. A., 1967. The gross response of an experimental tumour to single doses of X-rays. *British Journal of Cancer, 21*, 108–123.

Thrall, D. E., Gillette, E. L., and Dewey, W. C., 1975. Effect of heat and ionizing radiation on normal and neoplastic tissue of the C3H mouse. *Radiation Research, 63*, 363–377.

Yerushalmi, A., 1976. Treatment of a solid tumour by local simultaneous hyperthermia and ionizing radiation: dependence on temperature and dose. *European Journal of Cancer, 12*, 807–813.

Yerushalmi, A., and Har-Kedar, I., 1974. Enhancement of radiation effects by heating of the tumour. *Israel Journal of Medical Sciences, 10*, 772–776.

Book review

Radiology of the nose, paranasal sinuses and nasopharynx (Section 2: Golden's diagnostic radiology). By G. D. Dodd and B-S Jing, 1977, pp. xi+342, illus., (Williams & Wilkins Co., Maryland, USA.), $37.00.

This book forms another valuable addition to the Golden's Diagnostic Radiology Series. The authors clearly have a sustained interest and very wide experience in their field. Each section mentioned in the title reviews the radiological anatomy and radiographic technique, before discussing the clinical conditions which may arise and their differential diagnosis. The illustrations and drawings are excellent and are clearly labelled. The value of tomography is correctly stressed as the most important conventional radiographic investigation. It is a pity that computer tomography has had to be omitted since clearly it is having a dramatic effect in increasing our knowledge and diagnostic acumen in nose and throat radiology. It is however, not yet universally available and for some time many of us will have to rely on conventional techniques. In spite of this and the omission of the larynx from the book (the latter being discussed in another volume from the same publishers), this will be a valuable reference book, not only for radiologists and radiotherapists, but also for ENT surgeons.

V. Cope.

1979, *British Journal of Radiology*, *52*, 219–222 March 1979

The influence of blood flow on temperature distribution in the exteriorized mouse intestine during treatment by hyperthermia

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(*Received July, 1978*)

Abstract

The non-uniform effects of hyperthermia observed in mouse intestine when heating is achieved by immersion of an exteriorized loop of jejunum in a hot bath were quantified. Intestinal damage was assayed by crypt destruction and correlated with local temperature and distance from major mesenteric blood vessels.

The rate of rise of temperature during heating was much greater in regions far from blood vessels than in those close to vessels. Equilibrium temperatures in regions close to vessels were as much as 2°C below liquid bath temperature. Such temperature differentials agreed well with those predicted from the heterogeneity observed in crypt destruction. Both histological and thermometric data suggest that major blood vessels may influence tissue temperature over a distance of approximately 2 mm and, within this region, temperature gradients of 1°C per mm may exist.

These findings raise questions concerning the interpretation of previously reported data from water-bath heating of both tumours and normal tissues. They also emphasize the need for consideration of the influence of blood flow on heating patterns during hyperthermal treatment of patients.

Localized hyperthermia for cancer therapy and research has been induced by several methods including hot baths, microwaves and ultrasound. Since the effects of hyperthermia are critically dependent on temperature, information concerning temperature distributions in tissue is basic to any biological study. Water-bath heating has been used in many hyperthermia experiments because of its apparent simplicity. Researchers have often assumed that the tissues heated were at temperatures close to that of the water bath, or have measured the temperature at only one or two points. However, Robinson *et al.* (1975; 1978) have measured temperature profiles in tumours implanted on the flank or on legs of mice and heated by means of water bath, and found the temperature to be markedly dependent upon vascularity and distance from major blood vessels.

Merino *et al.* (1978) noted that when exteriorized intestine of mouse was heated there was a heterogeneous response, with the smallest effect in regions adjacent to the mesenteric blood vessels. They suggested that this might be due to local cooling. We observed similar heterogeneity in hyperthermal killing of crypt cells when heating was achieved by immersion of an exteriorized loop of the jejenum in Krebs-Ringer solution. The damage again appeared to be correlated with distance from the mesentery and presumably with distance from major blood vessels. We have investigated this finding in greater detail using both biological and physical measurements, in an attempt to quantify the effects of cooling by blood flow in this model tissue system.

Materials and Methods

Female CFLP mice (10–12 weeks old) were anaesthetized with sodium pentobarbitone at 0.07 mg/g body weight. A loop of jejunum approximately 10 cm long was exteriorized through a small incision in the peritoneal wall and immersed in Krebs-Ringer solution which was thermostatically controlled to within ±0.1°C of the required temperature.

For the histological assay, the heated portion of the intestine was marked with a small stitch before being replaced in the animal and the wound closed. The animal was sacrificed 24 hours later and the heated portion of the instestine fixed with Bouins solution. Treatment temperatures ranged from 42°C to 44°C and the treatment time was 30 minutes. Heat damage was quantified by counting the number of surviving crypts per 1000 μm of jejunal circumference. Figure 1 is a transverse section of jejunum showing the asymmetric distribution of crypts following a hyperthermal treatment of 43°C for 30 minutes.

Biological assays of thermal gradients along the circumference were determined by measuring, on magnified images, the distance across which gradients of biological damage could be seen and dividing these distances by both biological and physical estimates of the temperature differentials. (Distance was measured between points on the jejunal wall where thermal damage was first apparent and, moving further away from the mesentery, where no surviving crypt cells could be seen). To correct for possible space distorting artefacts in

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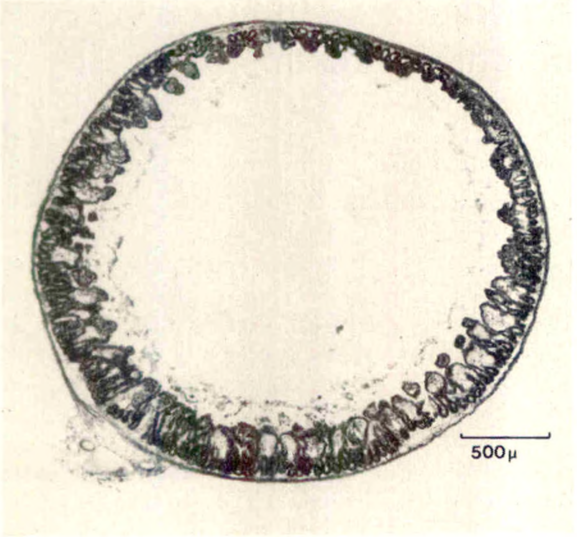

FIG. 1.

Transverse section of mouse jejunum stained with haematoxylin and eosin. The mouse was sacrificed 24 hours after a heat treatment of 43°C for 30 minutes.

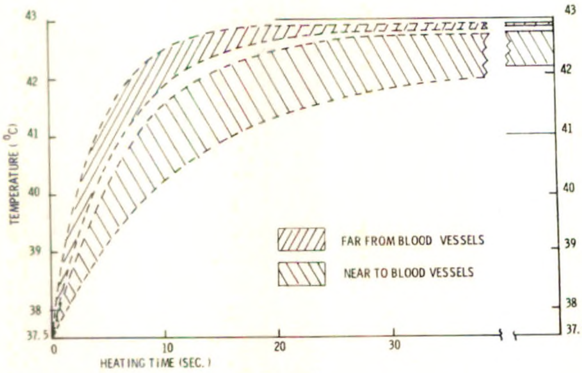

FIG. 2.

Temperatures near-to and far-from blood vessels in the jejunum as a function of time after immersion in Krebs-Ringer solution at 43°C. The hatched areas encompass the central 50% of the values measured.

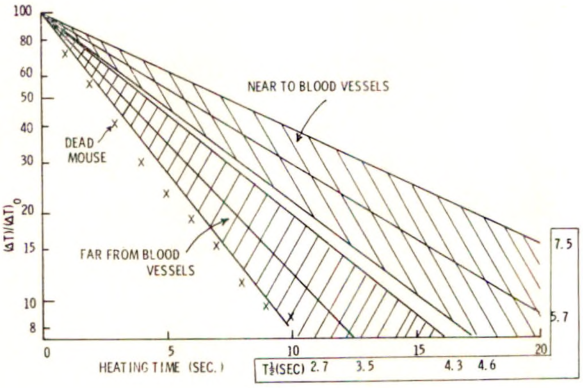

FIG. 3.

Heating rates of points near-to and far-from blood vessels in the jejunum. The ratio (×100) of the difference in temperature (ΔT) from equilibrium at any time post immersion to the value at time of immersion $(\Delta T)_0$ is plotted on a log scale against heating time. The hatched areas encompass the means and standard deviations of the values measured. Calculated values of $T_{1/2}$, the time for $(\Delta T)/(\Delta T)_0$ to be reduced to 1/2, are given along the bottom and right margin.

histological preparation, these distances were corrected by a factor corresponding to the ratio of the circumference of the sample in question to the average of all the sections measured.

For temperature measurements, copper-constantan thermocouples (100 µm in diameter) were inserted through the intestine either "near-to" or "far-from" mesenteric vessels.* The thermocouples were sutured in place and the exteriorized loop of the jejunum was immersed in Krebs-Ringer solution at a temperature of 43°C. Temperatures were monitored using a digital thermometer and strip-chart recorder from the time of immersion until near steady-state temperatures were attained.

RESULTS

Results of temperature measurements taken "near-to" and "far-from" the mesenteric vessels are summarized in Fig. 2. This is a plot of temperature *v.* heating time in Krebs-Ringer solution held at 43°C. To a close approximation, the difference between gut and bath temperatures decreases exponentially with time of immersion. The two shaded areas characterize the heating patterns for the two different regions in the gut. Regions "far-from" vessels heat more rapidly than regions "near-to" vessels. Since it is difficult to place and maintain thermocouples at specific locations in the gut, and since heating rates near-to vessels are more position-dependent than those far-from, there is a wider spread in the values near-to vessels. The hatched areas encompass the median and 50% of the measured values central to the median. There is some overlap of the data, but the equilibrium temperatures far-from the vessels are typically 0.1–0.2°C below bath temperature; those near to the vessels are much lower with one value at 41°C, *i.e.* up to two degrees centigrade below bath temperature.

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*It was estimated that "near-to" measurements were made within 0.5 mm of the mesenteric attachment. "Far-from" measurements were made diametrically opposite to the mesentery and over a range of ±0.5 mm.

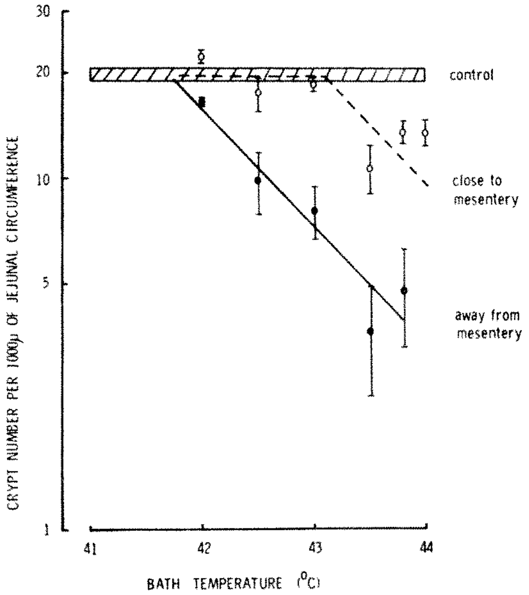

FIG. 4.

Effect of heating on crypt numbers close-to and far-from the mesentery, 24 hours after treatment.

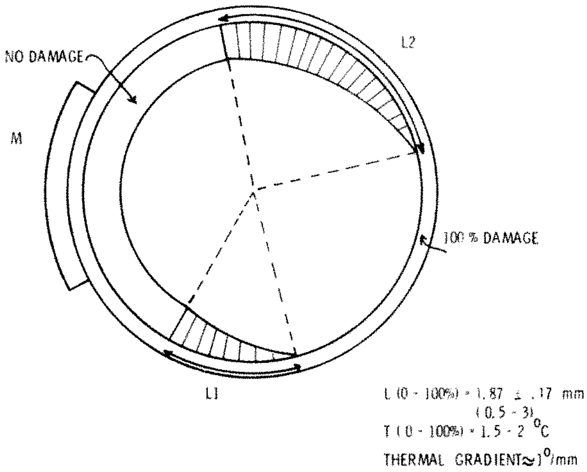

FIG. 5.

Schematic drawing of the gradient of thermal damage around the circumference of the heated gut. L1 and L2 are the distances around the circumference where a gradient of thermal damage could be seen.

The differences in heating rates are shown in Fig. 3 on which is plotted $(\Delta T)/(\Delta T)_0$, the ratio of the difference in temperature from equilibrium at any time post immersion, (ΔT), to the value at the time of immersion, $(\Delta T)_0$. The slopes of these lines represent the heating rates near-to and far-from blood vessels, and are characterized by the value of $T_{1/2}$, the times taken to reduce $(\Delta T)/(\Delta T)_0$ by one-half. The hatched areas encompass the means and standard deviations of the values measured. The mean values of $T_{1/2}$ were 3.5 seconds far-from the vessels and 5.7 seconds near-to the vessels. The X symbols in Fig. 3 represent heating data from a dead mouse with no cooling from blood flow.

Results of the histological assay for thermal inhomogeneity around the gut are shown in Fig. 4. This is a plot of crypt number per 1000 μm of jejunal circumference (log scale) for regions in the gut near-to and far-from the mesentery as a function of bath temperature.

Near to the mesentery there is little cell destruction after heating for thirty minutes at bath temperatures below 43.5°C. In regions away-from the mesentery, however, significant damage is apparent at a bath temperature of about 42.5°C. The data are consistent with temperature differences in excess of 1°C between regions near-to and far-from the mesentery, in agreement with the physical measurements of temperature in those two regions.

A schematic diagram of a cross section of the heated gut is shown in Fig. 5. The regions L1 and L2 on each side of the mesentery (M) illustrate the regions across which a gradient of thermal damage could be seen. The average of those measured lengths was determined to be 1.87±0.17 mm, with values ranging from 0.5 to 3 mm. This length, together with the biologically and physically estimated temperature differences of 1–2°C, suggests that thermal gradients of about 1°C/mm are present in the exteriorized gut during water bath heating.

DISCUSSION

Although the gut may present a rather extreme case with high rates of blood flow, our data clearly illustrate the effect which blood flow can exert on heating patterns and also the need for careful physical studies to support biological hyperthermia experiments. One of us has reported similar effects of blood cooling on the thermal pattern in tumours implanted on the legs of mice heated by a water bath (Robinson *et al.*, 1978). These studies raise questions concerning some of the experimental results reported with water-bath heating of both tumours and normal tissues where there is well defined vasculature. In addition they emphasize the need for careful studies on the role of blood flow on heating patterns in human patients treated with localized hyperthermia.

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We would like to thank Dr. S. B. Field and other colleagues at the Cyclotron Unit for helpful discussion.

REFERENCES

MERINO, O. L., PETERS, L. J., MASON, K. A. and WITHERS, H. R., 1978. Effect of hyperthermia on the radiation response of the mouse jejunum. *International Journal of Radiation Oncology, Biology, Physics, 4*, 407–414.

ROBINSON, J. E., MCCULLOCH, D. and EDELSACK, E. A., 1975. Estimation of tumor immersion technique for radiobiological hyperthermia studies. (Abstract). *Medical Physics, 2*, 159.

ROBINSON, J. E., HARRISON, G. H., MCCREADY, W. A. and SAMARAS, G., 1978. Good thermal dosimetry is essential to good hyperthermia reasearch. *British Journal of Radiology, 51*, 532–534.

Book reviews

Technical aspects of Tomography. By M. L. Durizch, pp. ix+210, illus., 1978 (The Williams and Wilkins Company, Baltimore, U.S.A.), $9.95.

This slim paperback volume has been designed as a tomographic reference manual for practising radiographers, with chapters dealing with the skull, chest, peripheral skeleton, the spine and soft tissue structures. It has been written by a very experienced technologist who punctuates the detailed text with additional hints and advice in a manner which emphasizes her enthusiasm for the subject. The description of each technique includes details of suggested tube movement, film size, projections, positioning, preliminary films and separation levels. The information is summarized in concise tabulations at the end of the chapter. The author stresses the narrow technical latitude between optimal and poor tomograms, and the need for the operator to have a sound knowledge of anatomy to achieve correct orientation of the sectional image levels. The chapter dealing with the skull is especially good with outlines of valuable additional projections to demonstrate areas not fully covered by the routinely accepted views.

The layout is clear and orderly with excellent accompanying illustrations of patient positioning and resultant radiographs. However, I found the juxtaposition of metric and American/British linear measurement instructions irritating and would have preferred a complete metric approach with bracketed imperial information. Many may not agree with some of the suggested tube movements; for example the use of pluridirectional motion for lung tissue is open to question. It is also a pity that the author has not recorded her attitude to and opinion of inclined plane techniques and of intensifying screen/film combinations including the rare earth phosphor screens. These are minor criticisms and do not detract from a book which would be a worthy addition to the work-bench in X-ray departments and to the libraries of schools of radiography for pre- and post-diplomate students.

JOHN PETERS.

Computed Tomography of the Human Body. An Atlas of Normal Anatomy. By R. J. Alfidi, J. Haaga, M. Weinstein and J. de Groot, pp. ix+197, 220 illus.,, 1977 (The C. V. Mosby Co., St. Louis, U.S.A.), £29·00.

Anatomy is basic to surgery and radiology, but axial anatomy was in the past only of passing interest. It was mainly relevant in providing a three-dimensional or in-depth view to relate structures to each other in the antero-posterior plane.

In computed tomography and ultrasonography, however, axial anatomy is all important. For radiologists, such a radical change can be quite disconcerting. Anatomy must literally be rediscovered.

There is yet another reason for the new spate of information on anatomy directed at the radiologist. Computed tomography shows soft tissue structures in great detail. Whereas previously the names of muscles could be ignored and the position of the peripheral nerves was largely irrelevant, the muscle bundles and intervening neurovascular bundles can now be visualized and, in radiology, what can be seen must have a name or an explanation.

The Cleveland team have been concerned with CT from an early stage of its development and have considerable experience. Their presentation takes the form of labelled comparisons of anatomical sections and CT prints with only a very short introductory text. The labelled anatomical photographs of the cranium are of high quality. There has, however, been no attempt to portray the innumerable variations of anatomical size and position and no explanation for the recognition of particularly difficult areas on the CT sections.

This book is produced with the minimum of fuss and bother and there are no unnecessary distractions. The relevant sections can be quickly located. Students will find the work quite valuable as a reference work for computed axial anatomy.

L. KREEL.

1979, *British Journal of Radiology*, 52, 223–225

Technical notes

New equipment for double contrast arthrography of the knee

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(*Received June, 1978*)

It has been recognized for some time that the best arthrograms of the knee are obtained when the position of the patient can be controlled by screening (Ricklin *et al.*, 1971; Butt and McIntyre, 1969) but this usually results in loss of definition when a routine undercouch tube is used.

A removable cassette tunnel is described that will fit a Siemens "Koordinat" table. Simple alteration in dimensions will allow fitting to any X-ray table. The routine arteriography apparatus is utilized with an overcouch high speed tube with a 0.6 mm focal spot and undercouch intensifier. High definition screens and film can be used with resulting high quality radiographs.

DESCRIPTION OF EQUIPMENT

Following description of a removable cassette tunnel (Peck and Butcher, 1974) it was felt that this could be modified to take eight coned radiographs of each meniscus in different degrees of rotation, and with a new addition to the tunnel, with different amounts of varus or valgus strain to "open out" the knee joint to give good apposition of air to both surfaces of the meniscus.

Roebuck (1977) stated that it is usually impossible to create enough strain to give a good air gap around the meniscus, particularly over the anterior horn. This problem has been overcome with the new equipment.

The removable cassette tunnel (Fig. 1) is fixed to the table utilizing the standard table rails. The tunnel which is constructed of high quality plywood has a central window (7×7cm) surrounded by lead. The tunnel is designed to accept a drawer in which a cassette (15×40 cm) and four wooden blocks are positioned (Fig. 2). The wooden blocks are moved after each exposure and therefore allow eight radiographs to be taken on one film. The drawer can be inserted into the tunnel from either side.

There are two flat padded plates mounted on adjustable rods, controlled by knurled knobs, fixed directly to the tunnel (Fig. 1).

TECHNIQUE

The tunnel is fixed to the table and the table is centred to the tube and intensifier using the cross wires incorporated into the central window. The table is then locked into position and not moved again. The tube is elevated to allow the patient to lie supine on the table for injection of air and contrast.

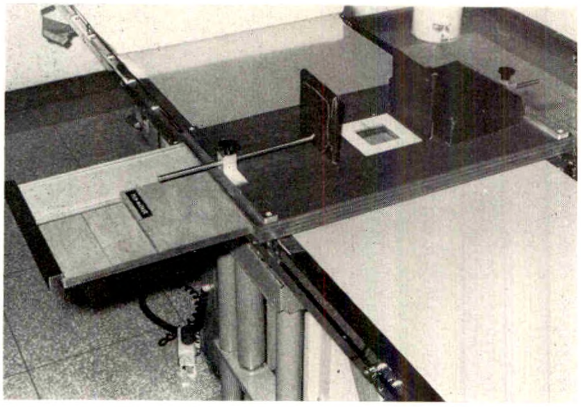

FIG. 1.

The cassette tunnel is fixed to the table with the drawer partly slid into position. The cross wires over the central window are an aid to centring.

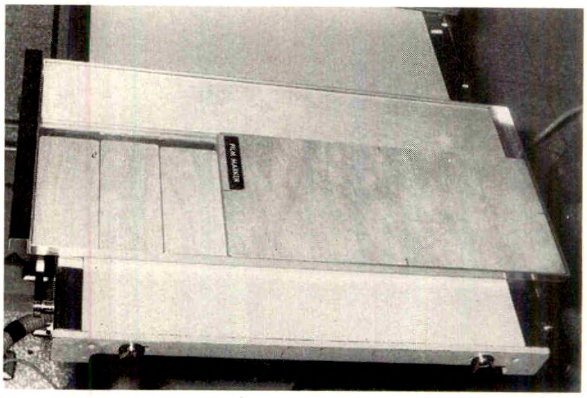

FIG. 2.

The drawer with the cassette and wooden blocks.

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Prior to injection of contrast a 5 cm crêpe bandage is applied above the patella to occlude the supra-patellar bursa. The knee is punctured. Synovial fluid is aspirated to reduce excessive dilution of the contrast. 5 ml of Dimer X (Roebuck, 1977) and sufficient air to distend the knee is injected. This usually requires about 50–80 c.c. of air. The needle is removed and a spray of Nobecutane used to seal the puncture site.

The knee is then flexed and extended several times and the patient turns prone with the relevant knee between the adjustable pads. The tube is lowered, and screening of the meniscus can begin with the radiologist rotating and adducting or abducting the knee exactly as required to demonstrate the menisci with a good air gap along their entire length (Fig. 3). The leg is rotated to the required position, strain applied and screening stopped. The drawer and cassette are slid into the tunnel and an exposure made. The drawer is removed and the leg rotated to the next position. This routine is continued until all the meniscus has been examined and radiographed. It is usual for a series of eight radiographs of each meniscus to be taken.

After the examination has finished the small bandage is removed which rapidly relieves the often uncomfortable distension of the knee joint. A 15 cm crêpe bandage is then applied for 24 hours and the patient warned of a possible slight stiffness and aching.

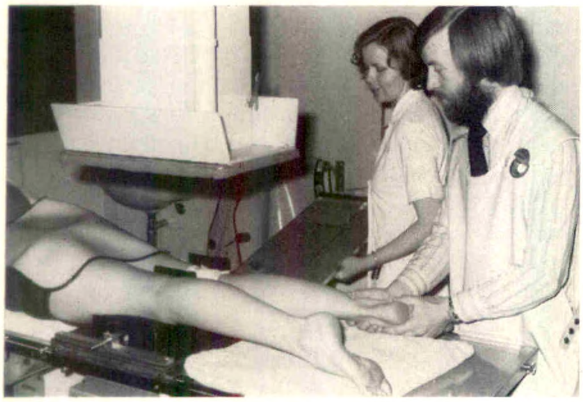

FIG. 3.

The patient lies prone and the leg rotated to the required position. (The tube has been raised for illustration purposes.)

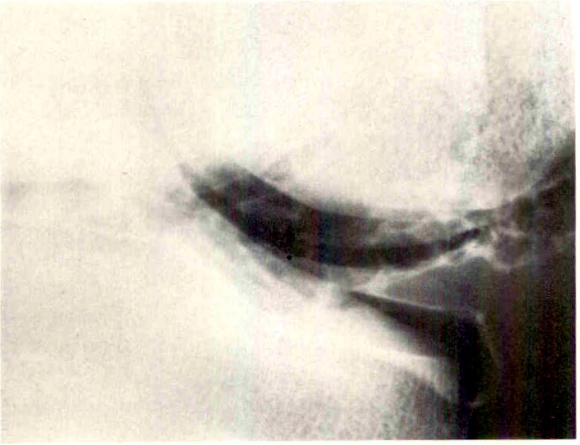

FIG. 5.

Normal lateral meniscus.

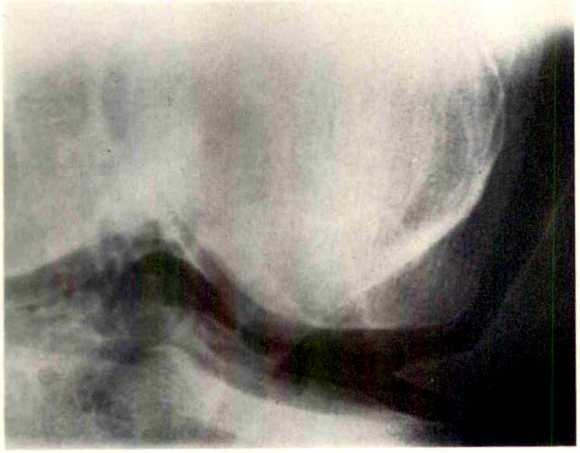

FIG. 4.

Normal medial meniscus.

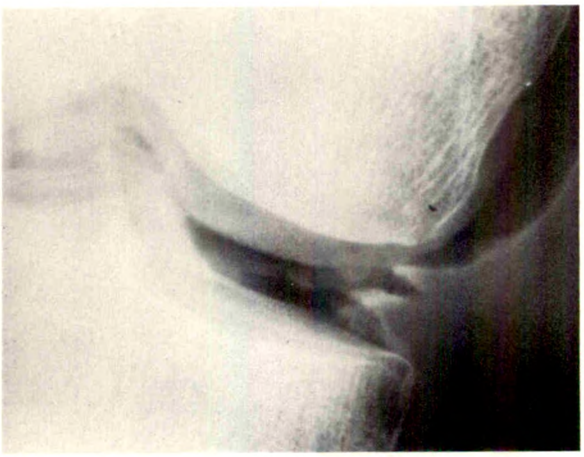

FIG. 6.

Tear of medial meniscus.

RESULTS

The quality of the radiographs obtained is high with a result that the number of arthrograms being requested has increased markedly. The need to repeat radiographs has been eliminated. No problems with the new equipment have been encountered.

Measurement of the total radiation dosage to the radiologist's hands after 20 examinations was less than 20 mrem and therefore insignificant.

Some examples are included (Figs. 4, 5 and 6).

CONCLUSION

A method of screening and taking high-definition radiographs of the menisci is described with a new technique for producing sufficient strain to examine the whole meniscus with true double contrast.

ACKNOWLEDGMENTS

I would like to thank the Physics Department, Westminster Hospital, who constructed the equipment to such a high standard and also Miss Hella Reickmann who developed the idea and worked out the radiography.

REFERENCES

BUTT, W. P., and McINTYRE, J. L., 1969. Double-contrast arthrography of the knee. *Radiology*, *92*, 487–499.

PECK, S. M. and BUTCHER, C., 1974. Apparatus for arthrography of the knee. *Radiography*, *470*, 46–47.

RICKLIN, P., RUTTIMANN, A., and DEL BUONO, M. S., 1971. In *Meniscus lesions; practical problems of clinical diagnosis, arthrography and therapy* (Grune and Stratton, New York).

ROEBUCK, E. J., 1977. Double contrast knee arthrography. Some new points of technique including the use of Dimer X. *Clinical Radiology*, *28*, 247–257.

Ultrasound equipment for intra-rectal imaging of the prostate

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Ultrasonic radial rectal scanning has been shown by workers in Japan (Watanabe 1971) and the USA (King *et al.*, 1973; Resnick *et al.*, 1976) to allow the identification of malignant change in the prostate with a high degree of accuracy. The apparatus used by Watanabe (1971), has become commercially available as the Aloka ASU–8M–C radial scanning chair. The apparatus facilitates the insertion of a transducer covered by a water bag into the rectum. The transducer is rotated by a motor drive and a radial scan of the pelvis is obtained.

Preliminary work in our department was carried out using the above chair connected to an Aloka SSD–60C B scanner. These items were kindly loaned by LKB Instruments Ltd. Unfortunately this arrangement gave bistable pictures which were not felt to be of sufficient diagnostic value. It was, therefore, decided to interface the scanning chair to the Nuclear Enterprises NE 4200 grey-scale B scanner in our department. This would probably be the arrangement favoured by most departments wishing to acquire the Aloka chair as an accessory.

This communication deals with the steps necessary to accomplish the interfacing and the results which may be expected.

Four stages may be identified in the interfacing:

(i) The rectal transducer must be connected to the NE 4200 electronics.

(ii) The sine and cosine signals from the chair must be substituted for those from the NE frame.

(iii) The transmitter delay must be adjusted to that appropriate to the chair.

(iv) A power source must be provided to drive the chair motor.

The connection of the transducer to the NE console is simply accomplished by attaching a cable from the receiver/transmitter sockets on the back panel to the socket on the rear of the chair.

The NE frame is connected to the console via a McMurdo 34-way plug inside the back panel. A new plug and shell are required* and a four core screened cable should be connected between the sine/cosine potentiometer in the chair and the appropriate pins on the new plug. Table I gives the connections. It is also an advantage to connect some resistors to the X, Y position pins so as to bring the beam to near the middle of the adjustment range on the B scan. Pins C9 and D3 are linked to select 2.5 MHZ on the receiver. If the 3.5 MHZ option is available then this should be used. Substitution of this new plug and cable for the standard one will connect the sine/cosine position signals from the chair to the console and select the appropriate frequency.

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*No. MP134 obtainable from ITT Electronic Services, Harlow, Essex.

1979, *British Journal of Radiology*, *52*, 226–231

TABLE I

Function	Pin
Sine	A4
Cosine	A6
+E	B1
−E	A9
Ground	A5
Link	D3 C9

The transmitter delay compensates for the transducer face being separate from the centre of transducer rotation. That is, it is a time after the start of the X and Y sweeps at which the transmitter is triggered. In the standard Nuclear Enterprises configuration it is appropriate to a distance of 60 mm. For the rectal transducer the distance concerned is the radius of the probe. The reduction of the delay is most easily accomplished by changing the value of the input resistor (R29) to the ramp generator (CM2) on the board PCB 675 in the console frame. A small SPDT switch mounted on the edge of this board can select either the standard or chair values. This may be switched when the multiway plug is changed. We found a reduction from 150 K to 14 K to be suitable.

The motor drive in the chair requires 100 volts AC power. We provided this from an isolating transformer connected to the NE mains supply.

In our experience the switching of the scanner from normal to chair operation may be accomplished in less than five minutes. Figure 1 illustrates the quality of the results obtained.

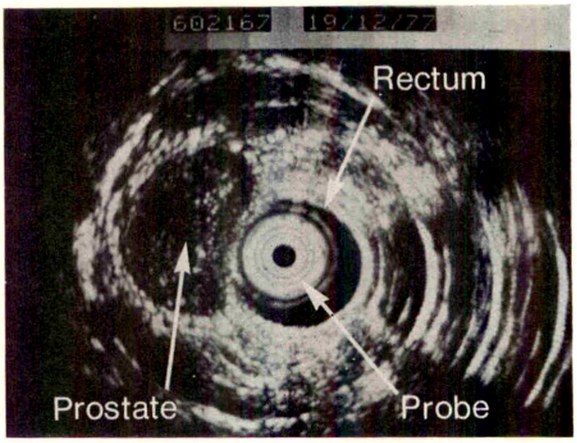

FIG. 1.

The transducer is seen within the rectum surrounded by the water bag and closely applied to the anterior wall of the rectum. The prostate is well outlined anterior to the probe, together with the muscles of the pelvic floor.

ACKNOWLEDGMENT

Thanks are due to the Equipment Research Committee of the Scottish Home and Health Department for the provision of funds to purchase the Aloka rectal scanning chair.

REFERENCES

KING, W. W., WILKIE-MEYER, R. M., BOYCE, W. H., and MCKINNEY, W. M., 1973. Current status of prostatic echography. *Journal of the American Medical Association*, *226*, 444–447.

RESNICK, M. I., WILLARD, J. W., and BOYCE, W. H., 1976. Ultrasonography of the prostate. Abstract. First meeting of the World Federation for Ultrasound in Medicine and Biology, San Francisco, USA.

WATANABE, H., 1971. Diagnostic applications of ultrasonotomography of the prostate. *Investigative Urology*, *8*, 548–559.

A data storage and retrieval system for clinical research in oncology

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(*Received March, 1978*)

In clinical research it is of the utmost importance to keep standards of treatment at the highest possible level. However, extracting data from the patient's file often involves much work and obtaining answers to questions may be very time consuming. A computer can be introduced to reduce the amount of this work to a minimum. In this paper a system will be described that can be easily used by non-computer experts for data entry and retrieval. It is designed in such a way that it can cope with many different research studies. No reprogramming is necessary for new applications. The system can be implemented on a dedicated computer having a FORTRAN compiler with overlay facilities, and may be run on a computer used for radiotherapy planning.

In the design phase the following requirements were specified for the system:

it should be modular so that changes and new programs can be inserted easily;

it should be easy to use by non-computer experts;

- it should be flexible so that it can be used for different diseases;
- it should contain a statistics package;
- it should have graphics possibilities;
- it should be fast so that it can be used in an interactive manner.

It was decided that the retrieval process should be facilitated by means of a keyword oriented language which should be easy to learn and use. Although systems (Ludwig and Bagshaw, 1975; Fayos, 1976; Glicksman and McShan, 1976) are known with which it is possible to do research on a large data base for epidemiological studies working with large computers, the possibilities of the system described here are similar, with the advantage that it can be used for in-house research studies on a small dedicated computer and on an interactive basis.

Design of System

In order to make the retrieval programs independent of the variables used in the study, a data definition language had to be designed. With the help of this language the user can enter the names of variables, together with their attributes (*e.g.* the position in the record, the symbolic description of the codes etc.). When this is done the computer knows where to find the value of each variable in the patient's record. With this knowledge it can display the names of the variables together with the possible input values on a display terminal for data entry

TABLE I

Part of the checklist used for patients suffering from larynx cancer

Academisch Ziekenhuis	−1− Ponskrt. no. [1]	1
Vrije Universiteit	Volgno. ☐☐☐☐	2– 5
Amsterdam		
Legend: NR = Not Recorded 0 = No 1 = YES / = "OR"		
CA. LARYNX		
1. Status No. [A] ☐☐☐☐☐☐ Registration No. V.U.	A ☐☐☐☐☐☐	6–12
2. Name of patient:		
3. Sex ☐ 1 = male 2 = female	☐	13
4. Birthdate ☐☐ day ☐☐ month ☐☐ year	☐☐☐☐☐☐	14–19
5. Diagnosis: Sq. Cell ca.		
6. Date of diagnosis ☐☐ day ☐☐ month ☐☐ year	☐☐☐☐☐☐	20–25
7. Grade ☐ 1/2/3/9	☐	26
7.1 Lymphocyte infiltrated ☐ 0/1/9	☐	27
7.2 Ca. in situ ☐ 0/1/2/9 2 = microscopic in situ changes present with frank \ca	☐	28
8. Type ☐ 1 = proliferative 2 = ulcer 9 = NR 3 = infiltrated 4 = combined	☐	29
9. Side 1 = left 2 = right 3 = both	☐	30
10. Site		
10.1 Glottic ☐ 1 = VC 1+2–4 2 = AC 1+3–5 3 = PC 1+2+3–6	☐	31
10.1.1 Glottic with extensions 0 = not with extens. 1 = supraglottic ☐ 2 = subglottic 3 = transglottic	☐	32
10.2 Supraglottic ☐ 0/1 = supraglottic only 2 = supragl. with glottic ext. 3 = " with glottic + subgl. ext. 4 = " with minor pharyngeal ext. 5 = " with gross pharyngeal ext.	☐	33

purposes. It also uses this information when the user asks questions about the data stored.

After the data have been entered the user can begin asking questions. Each question starts with a keyword. This keyword represents some function. The keyword ACTUA for example indicates that the user wants to obtain an actuarial table. Some keywords expect further information. The keyword DISPLAY for example expects the list of variables of which the values should be displayed on a terminal. Moreover, each keyword can be supplemented with a condition that defines a subpopulation by means of the IF clause *e.g.* DISPLAY AGE IF SEX .EQ. FEMALE.

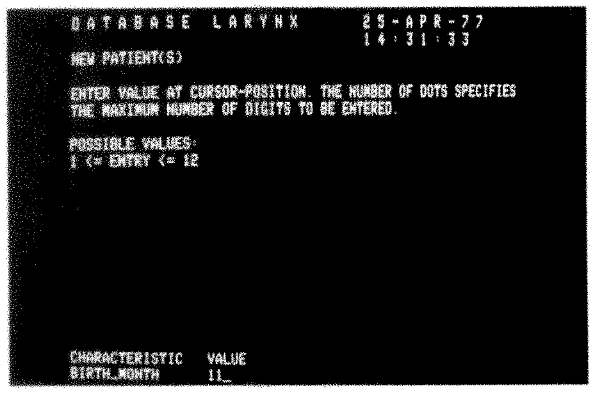
Since the symbolic description of the codes used is entered via the data definition language, the user can type in his own terminology (in the above example the word FEMALE was used instead of the code 2 that is actually stored in the computer memory). The keyword orientated language gives the user a powerful tool to browse through the data base. Since the process is interactive, the next question to be asked can be influenced by the results obtained earlier in the query session.

The data definition language

As indicated earlier the data definition language enables the user to specify the variables that he will use in his research project. These variables are written down on a checklist so that the corresponding values can be entered easily. In Table I part of the larynx checklist as used in Amsterdam is shown. This checklist is filled out by the radiotherapist. By means of the data definition language the information contained in the checklist (but not the actual values) can be specified. *e.g.* A/SEX/13, 1, 1, 1, 2 (1=MALE, 2=FEMALE). In this case the user tells the computer to add to the already existing list of variables the variable called SEX. Several attributes are then typed in: the values of this variable can be found starting in position thirteen (13) of the record. The value is contained in one position (1) and is of type integer (1). The lowest value possible is 1, the highest value is 2. For input and output purposes 1 stands for MALE and 2 for FEMALE. In this way the variable SEX is defined and this name can be used later on in the retrieval process because from now on the name is recognized by the system. All the variables of a checklist are defined in a similar way. This procedure has to be done once for each research study. Changes in names or attributes are always possible. In our case the data definition language is used only by the data base manager who sets up the data base in co-operation with the radiotherapist.

Data entry and verification

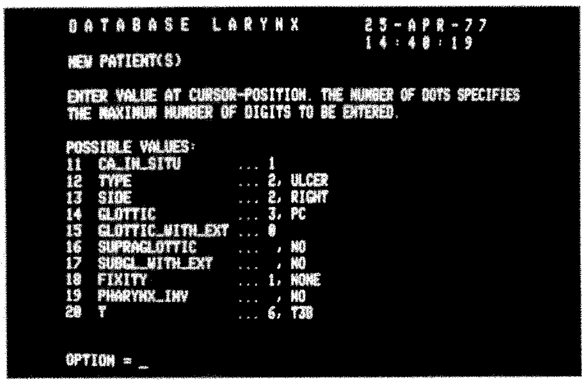
The data written onto the checklist can be punched or entered via a display terminal. In the latter case information is obtained from the data definition language about the names of the variables and their coding. An example is given in Fig. 1. Here the variable birth-month is asked for. In the display the range of values that can be entered is shown. For coded variables the codes and their symbolic descriptions are displayed. The input program then checks whether the entered data are within the specified bounds. If not, the word ILLEGAL ENTRY is flashed on the screen and a new value



```
D A T A B A S E   L A R Y N X        2 5 - A P R - 7 7
                                     1 4 : 3 1 : 3 3
NEW PATIENT(S)

ENTER VALUE AT CURSOR-POSITION. THE NUMBER OF DOTS SPECIFIES
THE MAXIMUM NUMBER OF DIGITS TO BE ENTERED.

POSSIBLE VALUES:
1 <= ENTRY <= 12









CHARACTERISTIC   VALUE
BIRTH_MONTH      11_
```

Fig. 1.

Example of the data entry function.



```
D A T A B A S E   L A R Y N X        2 5 - A P R - 7 7
                                     1 4 : 4 0 : 1 9
NEW PATIENT(S)

ENTER VALUE AT CURSOR-POSITION. THE NUMBER OF DOTS SPECIFIES
THE MAXIMUM NUMBER OF DIGITS TO BE ENTERED.

POSSIBLE VALUES:
11  CA_IN_SITU        ... 1
12  TYPE              ... 2, ULCER
13  SIDE              ... 2, RIGHT
14  GLOTTIC           ... 3, PC
15  GLOTTIC_WITH_EXT  ... 0
16  SUPRAGLOTTIC      ...  , NO
17  SUBGL_WITH_EXT    ...  , NO
18  FIXITY            ... 1, NONE
19  PHARYNX_INV       ...  , NO
20  T                 ... 6, T3B


OPTION = _
```

Fig. 2.

Example of edit phase of the data entry. Ten items of information that have been entered for a patient are displayed for checking and correction if necessary.

```
ACTUA IF GLOTTIC .NE. NO

                         ***     1 CASES WITH WRONG DATES    ***



YEAR  *ALIVE   *DIED    *LOST TO *WITHDRAWN*EFFECTIVE *ANNUAL*ANNUAL*CUMULATIVE
OF    *AT BE-  *DURING  *FOLLOW- *ALIVE DU-*NUMBER EX-*MORTA-*SURVI-*SURVIVAL
OBSER-*GINNING *INTERVAL*UP DU-  *RING IN- *POSED TO  *LITY  *VAL   *RATE UP TO
VATION*OF      *        *RING IN-*TERVAL   *RISK      *RATE  *RATE  *END OF
      *INTERVAL*        *TERVAL  *         *          *      *      *INTERVAL
*******************************************************************************
 0 - 1*    117.*      4.*      0.*       1.*      116.* 0.034* 0.966*     0.966
 1 - 2*    112.*      6.*      0.*       9.*      108.* 0.056* 0.944*     0.912
 2 - 3*     97.*      1.*      0.*      19.*       88.* 0.011* 0.989*     0.901
 3 - 4*     77.*      6.*      0.*      22.*       66.* 0.091* 0.909*     0.819
 4 - 5*     49.*      2.*      0.*      14.*       42.* 0.048* 0.952*     0.780
 5 - 6*     33.*      2.*      0.*      11.*       27.* 0.073* 0.927*     0.724
 6 - 7*     20.*      0.*      0.*       6.*       17.* 0.000* 1.000*     0.724
 7 - 8*     14.*      1.*      0.*       1.*       14.* 0.074* 0.926*     0.670
 8 - 9*     12.*      0.*      0.*       4.*       10.* 0.000* 1.000*     0.670
 9 -10*      8.*      0.*      0.*       2.*        7.* 0.000* 1.000*     0.670
   >10*      6.*      0.*      0.*       4.*        4.* 0.000* 1.000*     0.670
```

Fig. 3.

An actuarial table for patients with cancer in the glottic part of the larynx. An error in dates has been made in the data entry edit phase for one case and this is detected by the retrieval program. The program excludes this case from the actuarial analysis but does not identify it in the print-out.

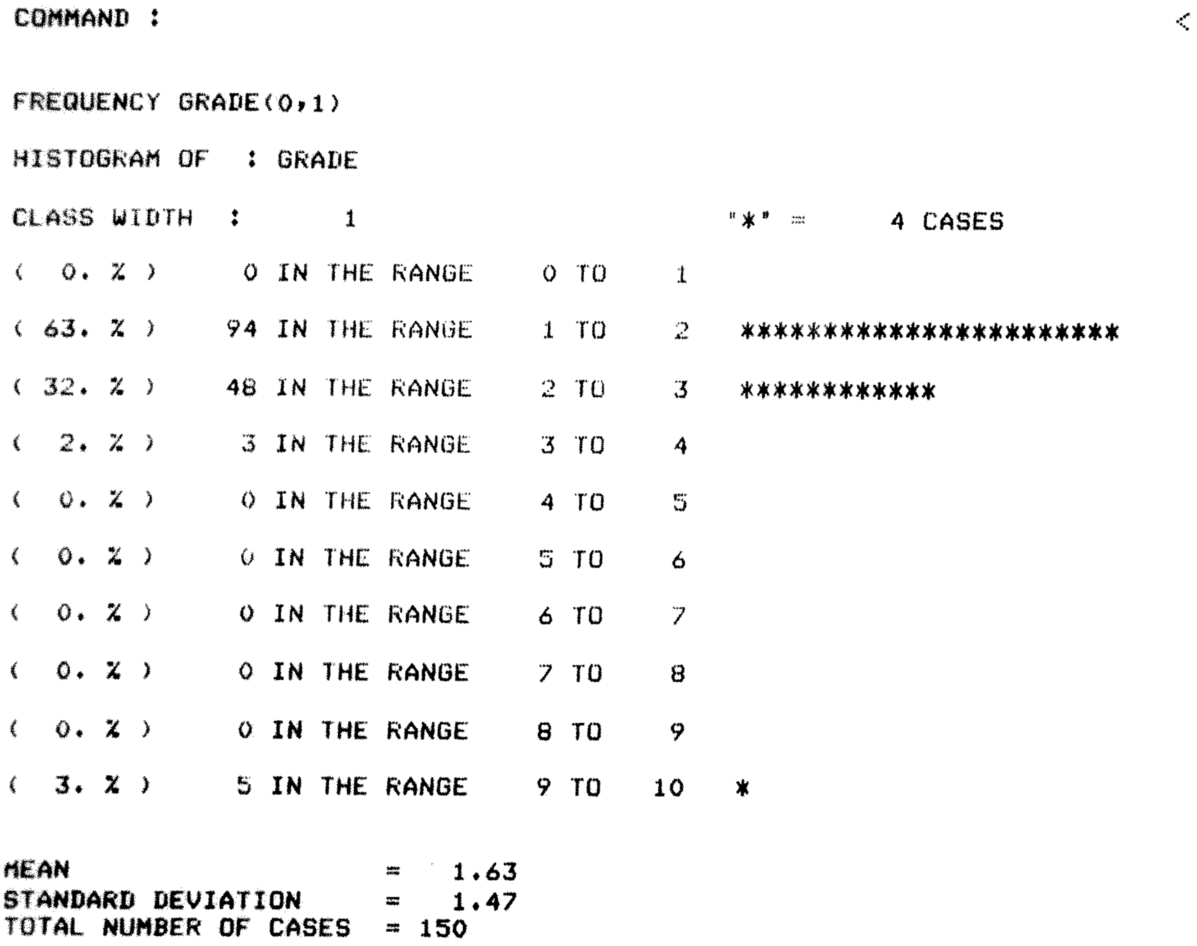
should be typed in. When the data of a patient are entered, the values of ten variables at a time are displayed for further editing (see Fig. 2).

The keyword orientated retrieval language

As already mentioned earlier, the language consists of keywords, each keyword specifying a separate function. The number of keywords can be easily extended to fulfil the needs of the radiotherapist. In our system most of the work can be done with about 15 keywords. When the user types in a question, the computer checks whether an IF clause was typed in. In that case those patient records are discarded that do not fulfil the conditions of the IF clause. Otherwise all patient records are screened. If one wants to obtain the actuarial survival table for a subgroup, the definition of the subgroup can be given via an IF statement. The actuarial table for patients with the tumour situated in the glottic part of the larynx is obtained by typing ACTUA IF GLOTTIC.NE. NO. The results of this are shown in Fig. 3.

As can be seen from Fig. 4, the distribution of a variable can be obtained through the keyword FREQUENCY. A table can be obtained with the keyword TABLE. Since the names of the variables are not allowed to be longer than sixteen letters, sometimes a shorthand is used. If one forgets what the abbreviation is, those names can be obtained that start with the letters that the user remembers, *e.g.* FIND AB is a command that returns all the variables starting with the letters AB. In order to reduce the amount of storage needed, the data have been coded. The variable SEX can have two values, coded 1 and 2. A separate dictionary is used to translate these codes into the symbolic descriptions MALE and FEMALE. In asking questions it is not necessary to remember the codes, since the system will translate symbolic descriptions into codes. Only the keywords TABLE and FREQUENCY require some knowledge about the codes since one has to specify the classwidth and the number of classes. The codes for the different variables can be obtained using the keyword DESCRIBE. Graphical output can be obtained by the PLOT command. Figure 5 shows the plot of an actuarial survival curve.

The query language is very easy to learn and enables the physician to obtain relevant information from the data base. The query language is used in an interactive way so that more precise questions can be asked after obtaining the answers to more general



```
COMMAND :


FREQUENCY GRADE(0,1)

HISTOGRAM OF   : GRADE

CLASS WIDTH  :       1                              "*" =      4 CASES

(  0. % )      0 IN THE RANGE     0 TO    1

( 63. % )     94 IN THE RANGE     1 TO    2   ***********************

( 32. % )     48 IN THE RANGE     2 TO    3   ************

(  2. % )      3 IN THE RANGE     3 TO    4

(  0. % )      0 IN THE RANGE     4 TO    5

(  0. % )      0 IN THE RANGE     5 TO    6

(  0. % )      0 IN THE RANGE     6 TO    7

(  0. % )      0 IN THE RANGE     7 TO    8

(  0. % )      0 IN THE RANGE     8 TO    9

(  3. % )      5 IN THE RANGE     9 TO   10   *

MEAN                     =   1.63
STANDARD DEVIATION       =   1.47
TOTAL NUMBER OF CASES    = 150
```

Fig. 4.
Example of a frequency distribution of the variable GRADE

questions. Subgroups can be easily specified and the questions posed after a subgroup has been defined refer to this subgroup until the subgroup definition is changed.

Statistical analyses may be performed using a small statistical package incorporated in the system. It is possible to carry out 2 × 2 and 2 × N contingency tests, Spearman correlation tests, Wilcoxon tests, rank tests and other analyses. A versatile tool for the radiotherapist or oncologist has thus been provided.

Discussion

The system was designed as a combined project of the departments of radiotherapy and medical informatics. It was made in such a way that each disease could have a separate checklist. A new project can easily be handled by the system and requires no reprogramming. In a separate paper the results of a study on the dose response in radiotherapy for laryngeal carcinoma are described using this system (Karim *et al.*, 1978). From this pilot study a lot of experience has been obtained. It was found that filling out checklists took the radiotherapist about ten minutes. The number of questions (variables) in the checklist was about 130. This number was so large because the checklist was used for research purposes. Since most information was initially obtained from the patient file, the data on

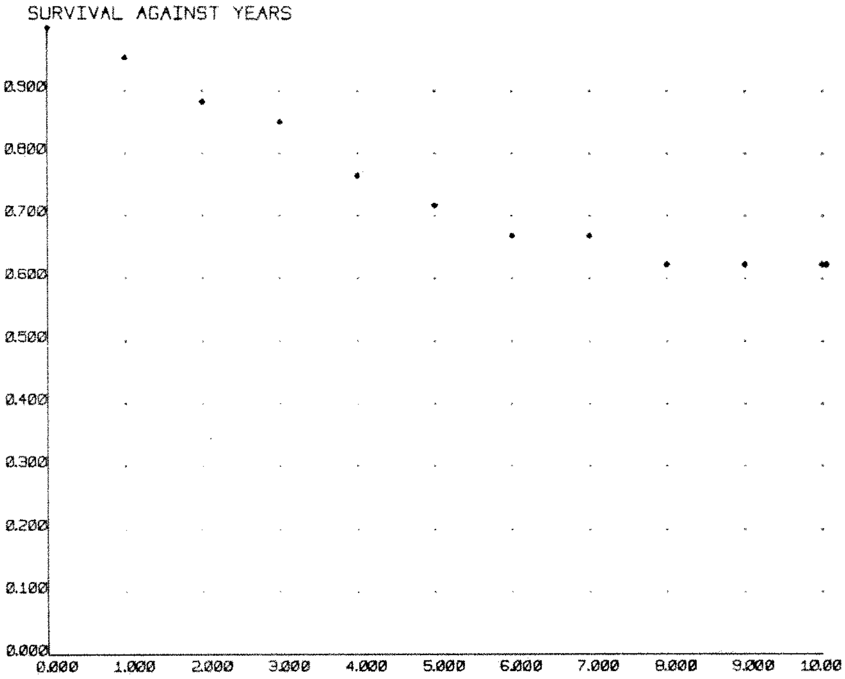


Fig. 5.
Plot of an actuarial survival curve.

the checklist have been punched on cards. Later on the data were entered into the computer directly via a display terminal by a clerk, although information via punched cards can still be handled as before.

With the help of the query language the radiotherapist could easily obtain quantitative answers to questions about age distribution, T and N staging differences in males and females, causes of local failures, types of complications, dose response relations, or duration of symptoms. The system can also be used for tumour registry purposes. Its main advantage lies in the fact that the clinician can obtain answers about a single patient or a group of patients in an interactive way within seconds. He does not need a large computer and the system can be implemented on a dedicated computer used for planning purposes.

REFERENCES

Fayos, J. V., 1976. Computerized radiation therapy data. *Cancer*, *37*, 2736–2745.

Glicksman, A. S., and McShan, D., 1976. Interactive computer based tumour registry in the State of Rhode Island. In *Computers in Radiotherapy in Europe*, *British Institute of Radiology*, *Special Report 13*, 27–28.

Karim, A. B. M. F., Snow, G. B., Hasman, A., Chang, S. C., Keilholtz, A. and Hoekstra, F., 1978. Dose response in radiotherapy for glottic carcinoma. *Cancer*, *41*, 1728–1732.

Ludwig, H. R., and Bagshaw, M. A., 1975. Progress towards an interactive decision system. In *Proceedings of the Fourth Conference on Computer Applications in Radiology* (*ACR*), Las Vegas, Nevada, 342–368.

1979, *British Journal of Radiology*, *52*, 232–235

Case reports

Erdheim-Chester disease associated with retroperitoneal xanthogranuloma

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In 1930 Chester, working with the Viennese pathologist Erdheim, described two patients with an unusual lipidosis showing distinctive bone changes. Sorensen (1964) described one patient with similar radiographic appearances and bone histology, and a fourth case was added by Jaffe (1972) who designated the condition "Erdheim-Chester disease". Histology showed granulomata containing lipid-laden histiocytes but the bone lesions differed from those seen in Hand-Schuller-Christian disease both in distribution and in the radiographic appearance. Similar histological appearances occur in retroperitoneal xanthogranuloma (Oberling 1935), but of the 36 cases of this condition described up to 1976, in only one (Melicow 1953) were bone lesions mentioned. We here report a further patient with Erdheim-Chester disease in whom autopsy revealed retroperitoneal xanthogranuloma, suggesting a common underlying pathology for these two rare conditions.

CASE REPORT

A 62-year-old male caucasian presented with a two week history of colicky lower abdominal pain, watery diarrhoea, anorexia, weight loss and hesitancy of micturition. There were no symptoms referable to his skeletal system. Examination showed only pallor and smooth enlargement of the liver. Haemoglobin was 8.8g/dl, ESR55mm/1hr (Westergren),blood urea 13 mmol/l, serum lipids and thyroid function tests were normal. Small bowel enema and sigmoidoscopy were normal. Barium enema showed tethering of the sigmoid loop in the right iliac fossa and distal diverticular disease. IVU showed bilateral hydronephrosis and hydroureter extending to the bladder, but no ureteric displacement.

Radiographs of the skull, lumbar spine, pelvis, ribs and carpal bones were normal. The long bones of all four limbs showed a widespread symmetrical abnormality. The entire diaphyses of both ulnae, radii, tibiae and fibulae, the distal halves of both femora and the proximal metaphyses of both humeri were involved. The abnormality consisted of an inhomogenous increase in bone density with thickening of trabeculae and loss of the corticomedullary junction. In the lower femora and upper tibiae there was apposition of perisoteal new bone. In the metacarpals and phalanges there was only a hazy increase in bone density affecting the diaphyses (Figs. 1–3). In all the affected bones the lesion appeared to end abruptly at the level formerly occupied by the epiphyseal plate, sparing the bone ends at the knees, ankles, shoulders, elbows and small joints of the hands.

At laparotomy there were many adhesions and marked inflammation of the serosa of the whole colon. No specific lesion was identified. Post-operatively the patient continued to have diarrhoea. He deteriorated mentally and despite intensive therapy died of bronchopneumonia five months after presentation.

At autopsy there was dense yellow fibrous tissue encasing both renal pelves, adrenals and extending up into the mediastinum. The ureters were not displaced. Histology of this material showed dense fibrosis with granulomata consisting of histiocytes with foamy cytoplasm with positive staining for fat (Fig. 4). The bowel was normal apart from some serosal thickening in the colon with some histiocytic infiltration. Sections of cancellous bone from the femur showed irregular thickened trabeculae. The intertrabecular spaces were filled with fibrous tissue with accumulations of foamy histiocytes and poorly defined granulomata (Fig. 5).

DISCUSSION

The bone lesions in Hand-Schuller-Christian disease are typically patchy and asymmetrical in distribution. The skull is commonly involved. Radiographic features indicate bone destruction, with

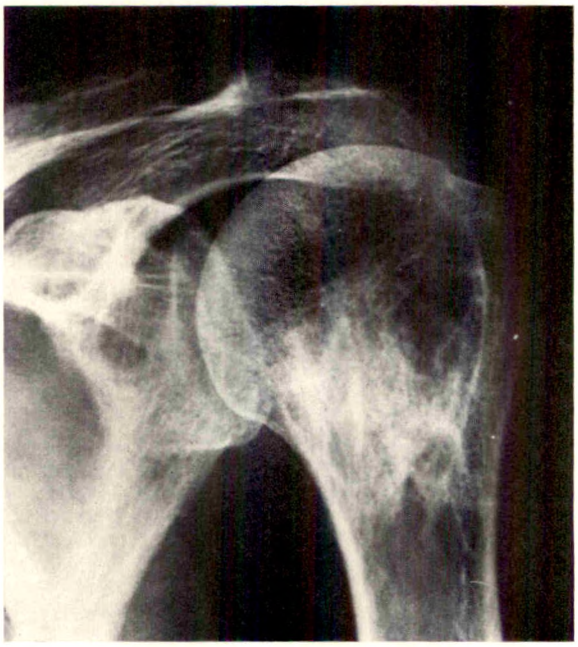

FIG. 1.

Left shoulder. Patchy sclerosis and coarsening of trabeculae of metaphysis and adjacent diaphysis of humerus with sparing of epiphysis.

Address for reprints: Dr. P. J. Robinson, Department of Radiology, St. James's Hospital, Leeds LS9 7TF, UK sclerosis occurring only during healing, especially after radiotherapy (Moseley 1962). The bone lesions of Erdheim-Chester disease differ both qualitatively and in distribution. Qualitatively, the affected areas show a patchy or diffuse increase in density with coarsening and irregularity of trabeculae in the medulla. The cortex appears thickened in some areas and where medullary sclerosis is marked the endosteal cortical margin is obscured. In Jaffe's case there was also cortical rarefaction in involved areas. Sorensen's case showed intersecting bands of sclerosis, irregular in size, thickness and direction, with areas of rarefaction between. Similar appearances are illustrated in radiographs of the excised tibia and fibula of Chester's case 1. The size and shape of the affected bones remains normal. Periosteal new bone formation was visible in our patient, but was not described in the previous cases.

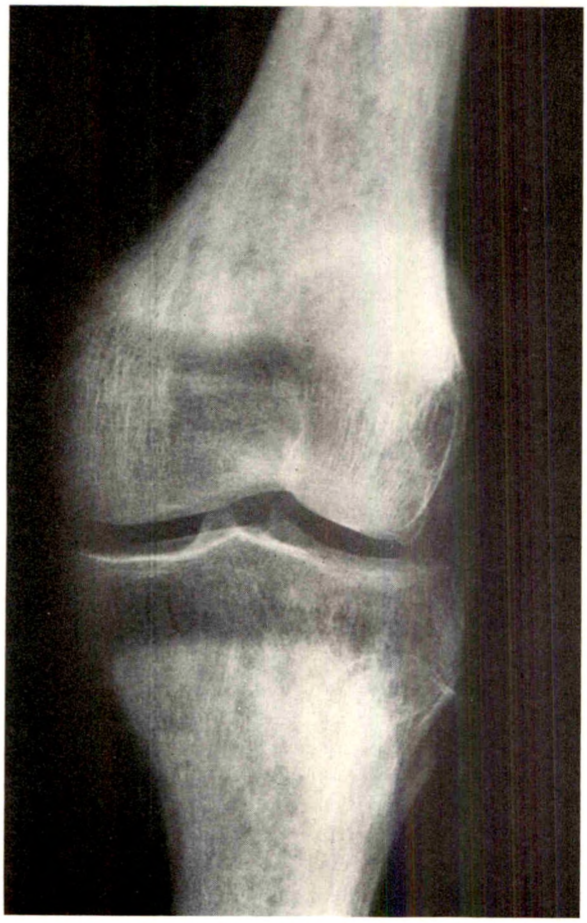

FIG. 2.

Left knee. Patchy sclerosis involving the metaphysis and diaphysis of femur and tibia. Epiphyses again spared. Periosteal new bone along femoral shaft.

The major long bones of the limbs are invariably affected. In Sorensen's case the humeri and femora showed the most severe lesions, but in all other cases the distal long bones were more severely affected. The axial skeleton appeared normal in our patient and in Jaffe's case. Chester's case 1 showed involvement of a single vertebral body and Sorensen mentioned minimal abnormalities in the spine and skull. Minor degrees of radiographic abnormality occurred in the metatarsals of our patient, in the

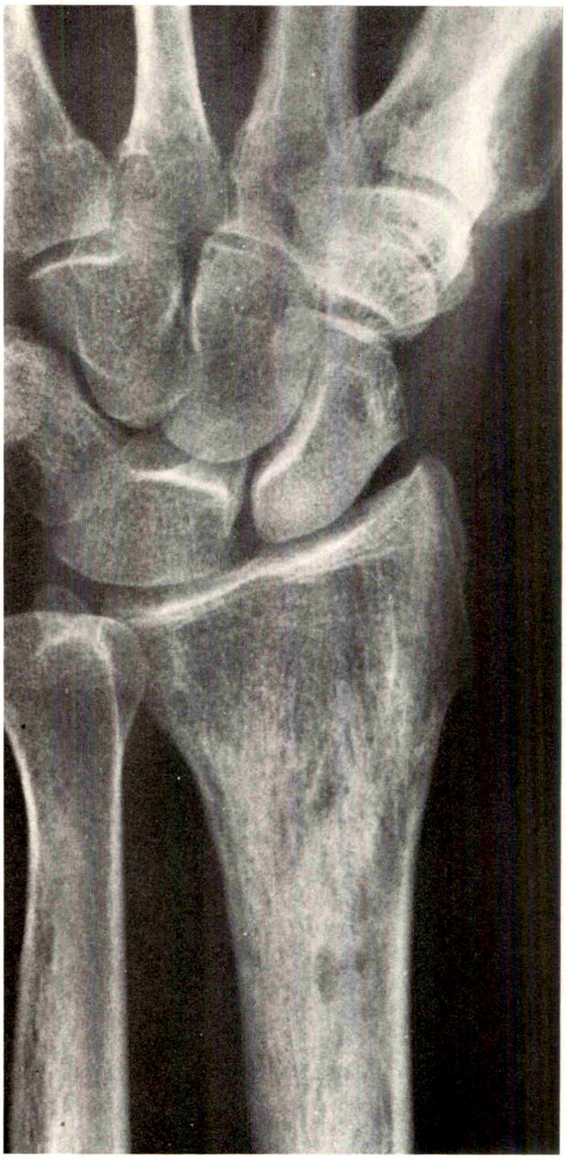

FIG. 3.

Right wrist. Patchy sclerosis of diaphyses and metaphyses of radius and ulna, with sparing of epiphyses. Carpal bones normal.

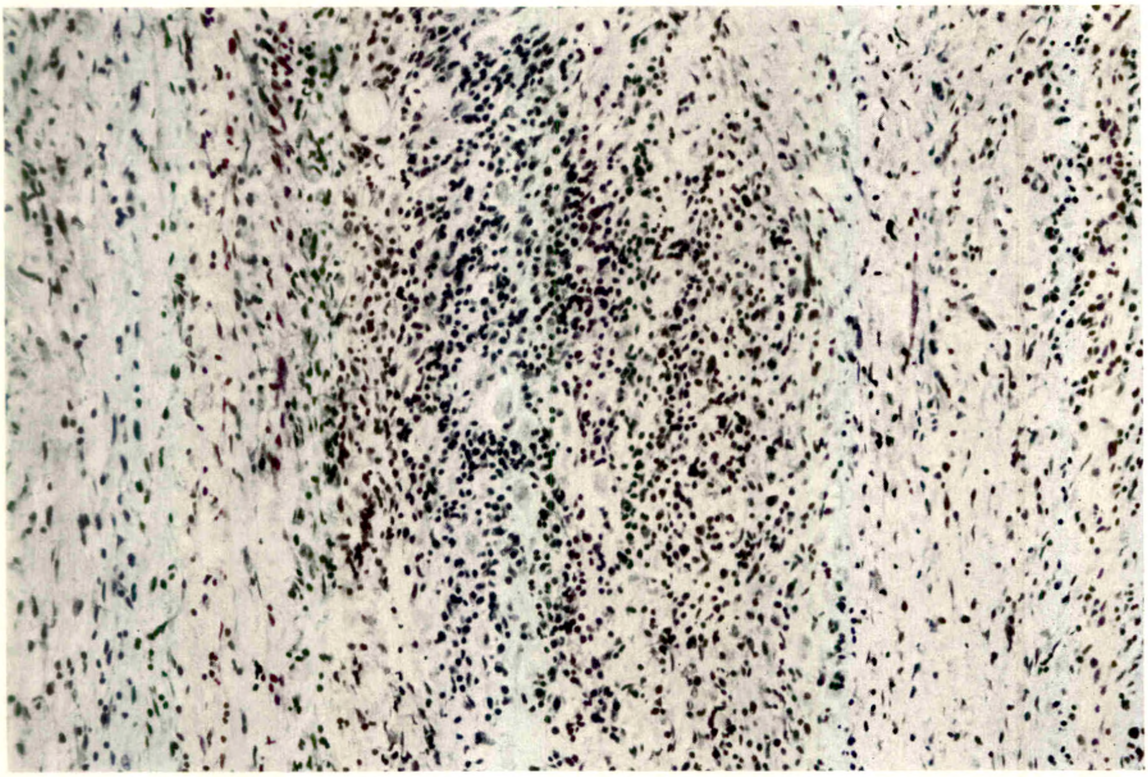

FIG. 4.
Granuloma in retroperitoneal tissue (H & E × 150).

metacarpals and tarsal bones of Jaffe's case, and in the pelvis, shoulder girdle and ribs of Sorensen's case. In all cases, however, the most marked lesions were those in the long bones.

The distribution of the lesions within these bones is characteristic. The metaphyses are invariably affected, and where the lesion is diffuse they show the most severe abnormality. In every case the epiphyses were either totally spared or affected to a far lesser degree than the adjacent metaphyses. Bone histology in our case showed changes similar to those described in detail by Chester (1930) and summarized by Jaffe (1972).

The condition of retroperitoneal xanthogranuloma first described by Oberling (1935) is also extremely rare. Kahn (1973) reviewed the literature and found 29 cases and described one more. Since then Gup (1972), Bissada and Fried (1973), Hou-Jensen *et al.*, (1973) and Ellis (1975) have reported single cases and Kyriakos and Kempson (1976) reported two, making a total of 36. The macroscopic and histological features of the retroperitoneal lesion in our case with dense fibrosis, granuloma formation and presence of foamy histiocytes are typical of retroperitoneal xanthogranuloma. The behaviour of the lesion varies from benign to frankly malignant (Kahn 1973). One case (Melicow 1953) had bony lesions which, from the brief description given, seem similar to those of our case. The retroperitoneal lesion seems distinct from idiopathic retroperitoneal fibrosis in distribution and histology (Mitchison 1970).

The occurrence of two such rare conditions in one patient strongly suggests that the underlying pathology is the same. Indeed, the histological features are identical and resemble those seen in Hand-Schuller-Christian disease, part of the group of diseases brought together by Lichtenstein (1953) as histiocytosis X. However, the radiographic changes in Erdheim-Chester disease are quite distinct from those seen in any of the described syndromes comprising histiocytosis X and retroperitoneal lesions are not described in these syndromes. We suggest that the two conditions found in our patient are

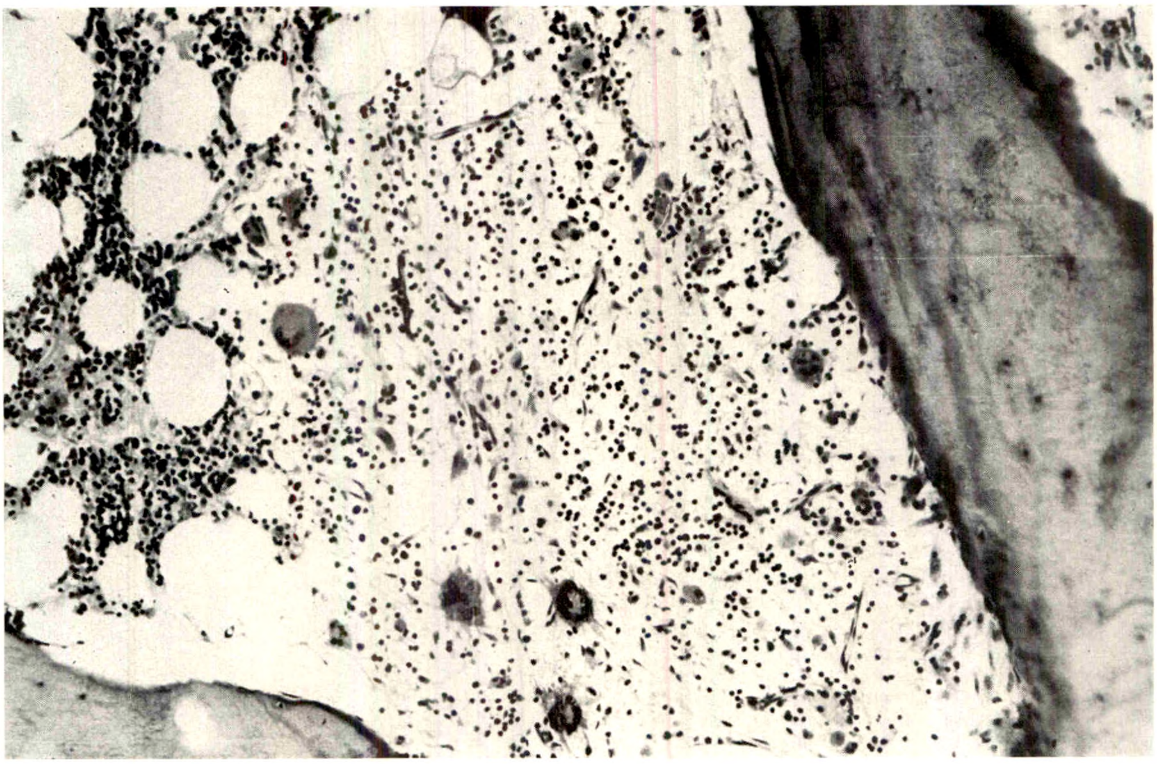

FIG. 5.

Cancellous bone from femur showing irregular trabeculae and foamy macrophages in intertrabecular spaces (H & E × 150).

manifestations of a single underlying pathology resembling Hand-Schuller-Christian disease but distinguishable on both clinical and radiological grounds. Although the bone lesions are asymptomatic we suggest that recognition of the characteristic radiographic appearances is helpful in what may be a difficult diagnostic problem.

REFERENCES

BISSADA, N. K., and FRIED, F. A., 1973. Retroperitoneal xanthogranuloma: case report and review of the literature. *Journal of Urology*, *110*, 354–356.

CHESTER, W., 1930. Uber lipoidgranulomatose. *Virchow's Archive Pathologische Anatomie und Physiologie*, *279*, 561–602.

ELLIS, H., 1975. Recurrent xanthogranuloma (malignant fibrous histiocytoma). *Proceedings of the Royal Society of Medicine 68* (*9*), 597–598.

GUP, A. J., 1972. Retroperitoneal xanthogranuloma. *Journal of Urology*, *107*, 586–588.

HOU-JENSEN, K., RAWLINSON, D. G., and HENDRIKSON, M., 1973. Proliferating histiocytic lesion (histiocytosis X) association of an extensive mediastinal and retroperitoneal sclerosing lesion with Gagel's granuloma of the posterior lobe of the pituitary. *Cancer*, *32*, 809–821.

JAFFE, H. L., 1972. In *Metabolic, Degenerative and Inflammatory Disease of Bone*. Lea and Febiger (Philadelphia), pp. 535–541.

KAHN, L. B., 1973. Retroperitoneal xanthogranuloma and xanthosarcoma (malignant fibrous xanthoma). *Cancer*, *31*, 411–422.

KYRIAKOS, M., and KEMPSON, R. L., 1976. Inflammatory fibrous histiocytoma. An aggressive and lethal lesion. *Cancer*, *37*, 1584–1606.

LICHTENSTEIN, L., 1953. Histiocytosis X. Integration of eosinophilic granuloma of bone, "Letterer-Siwe disease" and "Hand-Schuller-Christian disease" as related manifestations of a single nosological entity. *Archives of Pathology*, *56*, 84–102.

MELICOW, M. M., 1953. Primary tumours of the retroperitoneum. A clinicopathologic analysis of 162 cases, review of the literature and tables of classification. *Journal of the International College of Surgeons*, *19*, 401–449.

MITCHISON, M. J., 1970. The pathology of idiopathic retroperitoneal fibrosis. *Journal of Clinical Pathology*, *23*, 681–689.

MOSELEY, J. E., 1962. Patterns of bone change in the reticuloendothelioses. *Journal of the Mount Sinai Hospital New York*, *29*, 282–321.

OBERLING, C., 1935. Retroperitoneal xanthogranuloma. *The American Journal of Cancer*, *23*, 477–489.

SORENSEN, E. W., 1964. Hyperlipaemia; report of an unusual case complicated by bone lesions, macrocytic anaemia and leukoid bone marrow. *Acta Medica Scandinavica*, *175* (*2*), 207–214.

1979, *British Journal of Radiology*, *52*, 236–237

Intracranial aneurysm associated with cerebrovascular moyamoya disease. Report of a case and review of 13 cases

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Recently interest has increased in cerebrovascular moyamoya disease (Suzuki and Takaku, 1979; Krayenbühl, 1975), spontaneous occlusion of the circle of Willis (Kudo, 1975) or cerebral basal *rete mirable* (Nishimoto and Takeuchi, 1968). Kodama and Suzuki (1978) have reported five aneurysms in 35 adults with this condition, suggesting a high incidence and a specific location of the aneurysm in moyamoya disease.

A case of basilar artery aneurysm associated with this disease and a review of 13 aneurysm-associated cases reported up to now in Japan constitute this report.

Case Report

A 54-year-old woman was admitted soon after an episode of subarachnoid haemorrhage on May 2, 1977. Physical examination disclosed no neurological deficit but there was meningeal irritation and lumbar puncture showed bloody CSF.

Serial magnified angiography was performed by transfemoral catheter technique. The left internal carotid artery was nearly occluded at the bifurcation just distal to the posterior communicating artery. Abnormal fine vessels were demonstrated in the basal ganglionic region. The middle cerebral artery was filled through colaterals from the orbital artery in the late arterial phase. Transdural anastomosis with the frontal branch of the superficial temporal artery was also shown (Fig. 1). Right carotid angiography showed almost identical findings (Fig. 2). Vertebral angiography demonstrated a saccular aneurysm, approximately 4 mm in diameter, at the distal end of the basilar artery. Leptomeningial anastomosis through the posterior choroidal artery to the middle cerebral artery was revealed (Fig. 3). It was not possible to determine which of the vascular lesions was responsible for the subarachnoid haemorrhage on clinical or angiographic evidence.

The patient had a prolonged episode of angina pectoris from the 20th hospital day but recovered within a week. She was discharged improved on June 16, 1977.

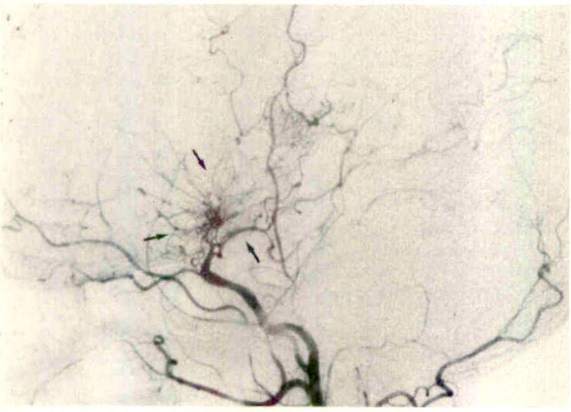

Fig. 1.

Lateral view of the left carotid angiogram. Intracranial portion of the internal carotid artery is narrow and almost occluded at the bifurcation. Abnormal fine net-like vessels shown in the basal ganglionic region (arrows).

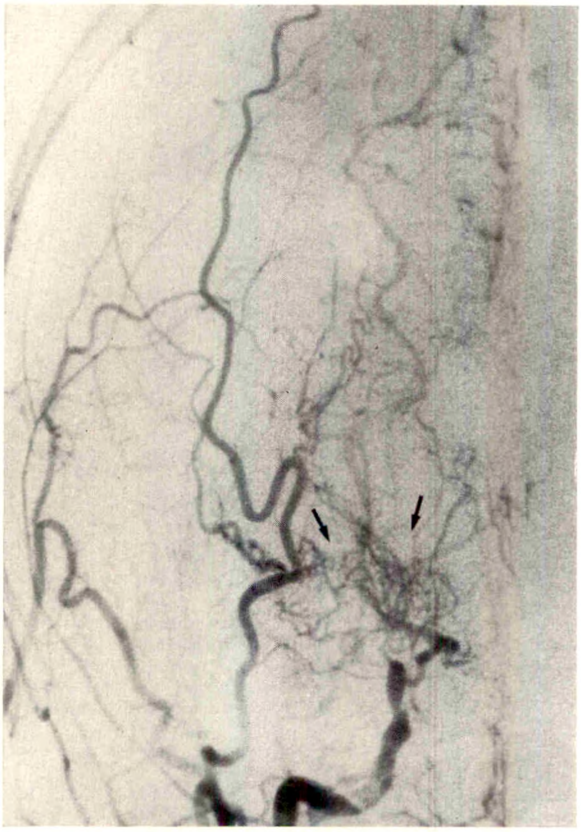

Fig. 2.

Antero-posterior view of the right carotid angiogram. There is occlusion of the internal carotid artery at the bifurcation with moyamoya blood vessels (arrows).

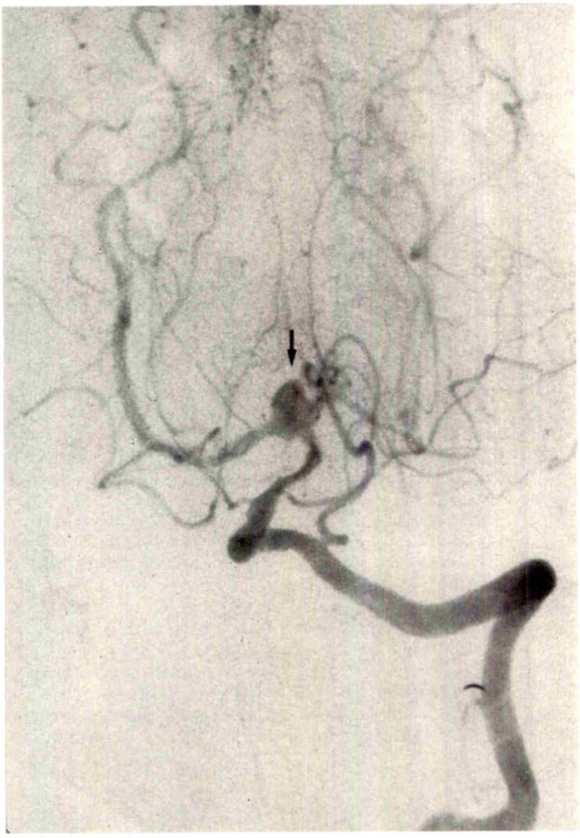

FIG. 3.

Antero-posterior view of the vertebral angiogram. A saccular aneurysm is pointed by arrow.

DISCUSSION

Out of 13 cases of aneurysm associated with moyamoya disease reported in Japan, seven were male and six female. Twelve cases were over 15 years old, the age range being from seven months to 59 years.

Location of the aneurysm was the basilar artery in three, the posterior choroidal artery in four and the anterior choroidal artery, the anterior communicating artery, the middle and the posterior cerebral artery each in one case. Thus the aneurysm was located on the vertebro-basilar system in seven out of 13 cases. In two cases, the aneurysm was related to the abnormal fine network of moyamoya blood vessel. Multiple aneurysms of the basilar artery were demonstrated in one case.

Aneurysms on the peripheral portion of the posterior choroidal artery and the moyamoya blood vessels are presumed to be pseudoaneurysms, because of their location and transient appearance in follow-up angiography (Kodama and Suzuki, 1978). However, haemodynamic changes in the posterior circulation due to gradually progressing stenosis or occlusion of the anterior part of the circle of Willis, could cause formation or growth of aneurysms on the vertebrobasilar system.

It is well known that moyamoya disease may present with subarachnoid or intracerebral haemorrhage. The initial symptom in all except one of the aneurysm-associated cases was subarachnoid heamorrhage; the exception had frequent fainting episodes.

It is important from the clinical point of view to determine which lesion is responsible for the haemorrhage, the aneurysm or moyamoya vessels. However, the responsible lesion could not be clearly established in the 13 reported cases, except one of ruptured aneurysm of the posterior choroidal artery, which resulted in intraventricular haemorrhage.

In fact, it is difficult in aneurysm-associated moyamoya disease to detect the responsible vascular lesion, if there is no clear neurological deficit corresponding to the ruptured aneurysm, and if angiographically there are no marked vascular changes due to aneurysmal rupture. Further studies including CT scan or autopsy are required.

REFERENCES

KODAMA, N. and SUZUKI, J., 1978. Moyamoya disease associated with aneurysm. *Journal of Neurosurgery, 48,* 565–569.

KRAYENBÜHL, H. H., 1975. The moyamoya syndrome and the neurosurgeon. *Surgical Neurology*, 353–360.

KUDO, T., 1975. *A Disease with Abnormal Intracranial Vascular Networks* (Igaku-shoin, Tokyo).

NISHIMOTO, A. and TAKEUCHI, S., 1968. Abnormal cerebrovascular network related to the internal carotid arteries. *Journal of Neurosurgery, 29,* 255–260.

SUZUKI, J. and TAKAKU, A., 1969. Cerebrovascular "moyamoya" disease; a disease showing abnormal net-like vessels in base of brain. *Archive of Neurology, 20,* 288–299.

1979, *British Journal of Radiology*, *52*, 238–241

Case reports

Clear cell sarcoma of tendons and aponeuroses treated with bleomycin and vincristine

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Clear cell sarcoma of tendons and aponeuroses is a rare tumour first described by Enzinger in 1965. A case is reported which responded to bleomycin and vincristine. Such a response has not previously been documented.

CASE REPORT

The patient was a 30-year-old woman who first presented in June 1975 with painless lumps on her left leg. Seven years previously she had received a slight knock to her left shin and then noticed two firm lumps at the site. Two years before presentation the lumps had increased in size and there was a generalized swelling of the leg below the lumps. Her appetite had diminished and she had begun to lose weight and experience pain in her left knee and ankle. For the last six months the area around the lumps had become red and hairless. Five weeks before presentation a new lump had appeared below the first two.

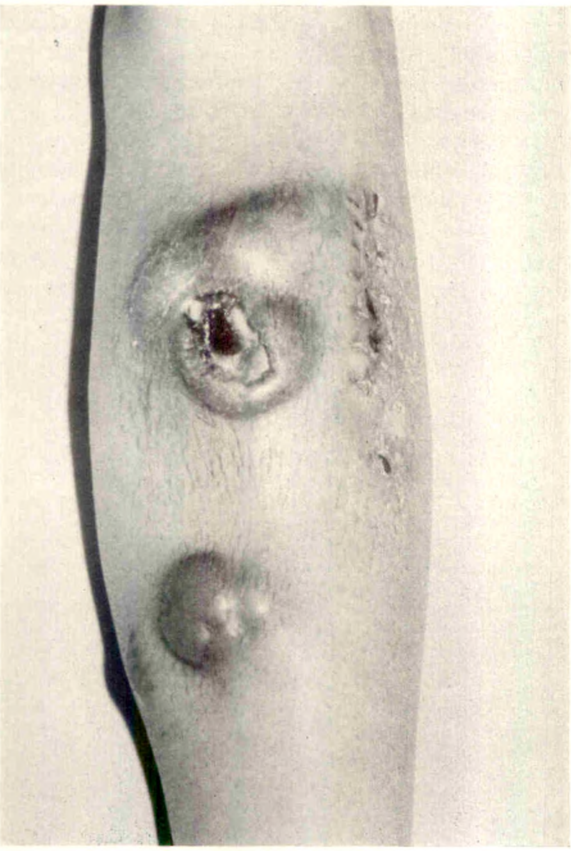

FIG. 1.

Photograph of left leg at presentation.

On examination she was found to have a mass over the upper third of her left tibia (Fig. 1.) measuring 10 × 8 cm with an ulcerated centre 3.5 × 2 cm and below this two further masses 4 × 3 cm and 1.5 × 1.5 cm. The masses were firm and appeared attached to the underlying bone. The left leg distal to the masses was swollen and oedematous so that the circumference of the left leg was 9 cm greater than the right measured at a point 10 cm below the patella. The skin over the masses was hot, red, and atrophic and there was wasting of the left thigh muscles. She had no palpable lymph nodes at this time. An X-ray of the left leg showed a well circumscribed lobulated soft tissue mass with a periosteal reaction along the shaft of the tibia. The radiologist's opinion was that this was a primary soft-tissue tumour secondarily involving bone and probably a liposarcoma. An open biopsy was taken and a diagnosis of clear-cell sarcoma was made. A lymphangiogram showed no lymphatic involvement.

Treatment and Progress

From July 28 to August 26, 1975 she received a course of radiotherapy to her left leg (Table I). There was rapid regression of the tumour and at the end of the course she was left with an ulcer which in turn had healed by December 1975.

She was well until August 1976 when she presented with a mass in the left femoral triangle. A drill biopsy revealed lymph node infiltration with sarcoma but a further lymphangiogram showed no other lymphatic involvement. This deposit proved to be the first in a series of further metastases in the right supraclavicular fossa, right thigh, abdomen, and right temple over the period from August 1976 to May 1977. These were treated as they arose with individual courses of radiotherapy (Table I). All the metastatic deposits regressed rapidly and completely by the end of each course of radiotherapy.

On June 10, 1977 she was readmitted with a pathological fracture of her right femur at the upper third of the shaft. She was also found to have multiple deposits in her scalp, right humerus, right cheek, and right cervical nodes.

Her blood count showed a haemoglobin of 7.9 g/dl, a white cell count of 4.4×10^9/litre and platelets of 76×10^9/litre. The thrombocytopenia deepened to 44×10^9/litre by June 15, 1977.

Pending internal fixation of the fracture a Steinmann pin was inserted, the fracture was stabilized with traction, and she was transfused with blood.

She continued to experience severe pain particularly at the fracture site and in the deposits in her neck with signs of peripheral nerve compression at the latter site. She required 20 mg of diamorphine orally every four hours for adequate analgesia.

In view of her thrombocytopenia further radiotherapy was contraindicated but the tumour was obviously very radiosensitive and it appeared likely that it might also prove responsive to chemotherapy. It seemed necessary to select

TABLE I

Schedule of radiotherapy

Date	Length of RT (days)	Radiation	Site	Dose (rad)	Number of fractions
1975					
28/7	29	8MV x	Left leg	4000	20
1976					
20/9	30	8MV x	Left groin	4000	20
15/12	34	8MV x	Mediastinum, bilateral axillae, supraclavicular fossae, and cervical nodes	4000	20
1977					
6/4	26	8MV x	Right hip	3200	16
3/5	13	8MV x	Abdomen	900	9
13/5	5	8MV x	Left side of neck	2000	4
18/5	5	10MeV electrons	Right temple	2000	4
28/10	13	^{60}Co γ	Skull	3000	10
3/11	11	300 kV x	Lumbar spine	1600	8

agents of low myelosuppressive activity. High dose bleomycin and vinca alkaloids as described by Samuel *et al.*, (1976) were chosen as a suitable basis for treatment. It was proposed to give her 2 mg of vincristine as a bolus intravenously followed by 90 mg of bleomycin as an intravenous infusion over 72 hours.

She started the first course on June 17, 1977 but there was a severe reaction to the bleomycin which was discontinued after only 20 mg had been given. Nevertheless a dramatic response was achieved in that all the tumour masses had become impalpable within fourteen days. Her general condition also improved considerably and her analgesic requirement fell so that she could be weaned off the diamorphine entirely.

She had two further courses of chemotherapy which included bleomycin to full doses (the first under steroid cover) and had improved sufficiently by August 1977 to have an operative internal fixture of the fracture of her femur. She was discharged home in October 1977 by which time she had received a total cumulative dose of bleomycin of 200 mg.

On October 21, 1977 she was readmitted complaining of headaches, diplopia, and difficulty in walking. On examination she had a partial third nerve palsy on the left side, saddle anaesthesia and absent ankle jerks. Apart from the neurological involvement she also had two new deposits in her scalp. Two days after admission she developed signs of meningeal irritation with neck stiffness, vomiting and photophobia. There were no localizing signs, no papilloedema and no neoplastic cells or evidence of infection in the CSF.

A diagnosis of intracranial and cauda equina deposits was made. She was given dexamethasone and commenced a course of radiotherapy (Table I.). The meningism and headaches disappeared and her third cranial nerve palsy improved by the end of the course.

She died at home in December 1977 and no post mortem was obtained.

Pathology

Biopsy material from the left leg comprised several fragments of soft uniformly grey tissue, the largest measuring 1.5 × 1.5 × 1.3 cm. On microscopy the tumour was made up of oval or epithelioid uniform cells with vesicular nuclei containing prominent nucleoli and pale cytoplasm (Fig. 2). The matrix between these cells was collagenous with areas of vacuolated myxoid material. Occasional abnormal mitoses were present among the clear cells and there was a small round cell infiltrate of varying density throughout. There were diastase-sensitive, periodic acid Schiff (PAS) positive granules in the cytoplasm of the tumour cells. A reticulin stain showed an alveolar-like pattern around nests of clear cells (Fig. 3). The Schmorl and Masson-Fontana reactions were negative. A diagnosis of clear cell sarcoma of tendons and aponeuroses was made.

A drill biopsy from a mass in the left femoral triangle showed lymphoid tissue containing tumour having appearances similar to that described above apart from the fact that the alveolar pattern in the reticulin stain was not marked. A further drill biopsy of a mass in the supraclavicular fossa showed fragments of tumour containing clear cells and with an alveolar arrangement in the reticulin stain. This was diagnosed as recurrent clear cell sarcoma.

Discussion

Clear cell sarcoma of tendons and aponeuroses is a rare condition. Enzinger (1965) reported 21 cases, two of which were from Bennett's series (Bennett 1947), and only 17 cases have been reported since—Kubo (1969), Dutra (1970), MacKenzie (1974), Bearman *et al.*, (1975) and Tsuneyoshi (1975).

It has been suggested that clear-cell sarcoma of tendons may be a melanin-containing tumour and that there may be an entity "malignant melanoma of soft tissue" which is distinct from clear-cell sarcoma (Kubo 1969, Tsuneyoshi 1976, Bearman *et al.*, 1975 and MacKenzie 1975.) We were unable to show the presence of melanin in our case.

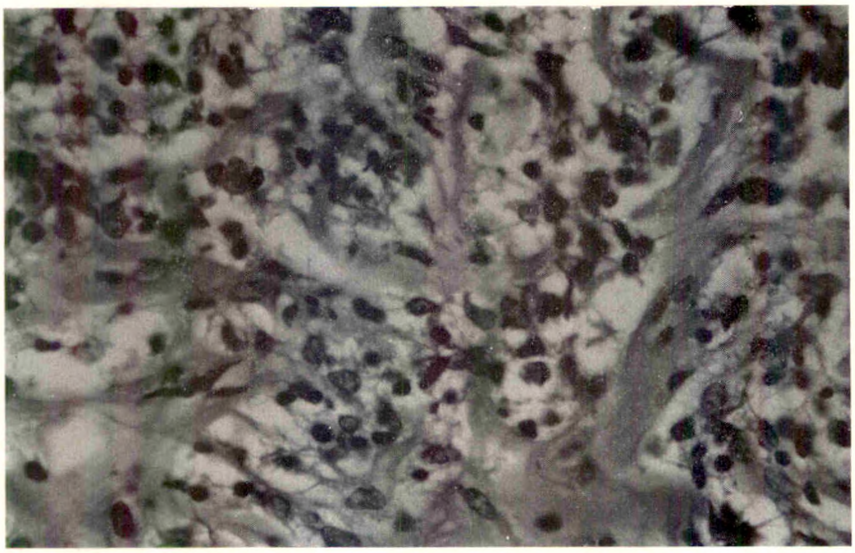

Fig. 2.

Photomicrograph of the tumour, showing cells with indistinct pale cytoplasm and prominent nucleoli. A moderate number of small round cells is also present. Strands of fibrous tissue are present.
(haematoxylin-eosin, × 500)

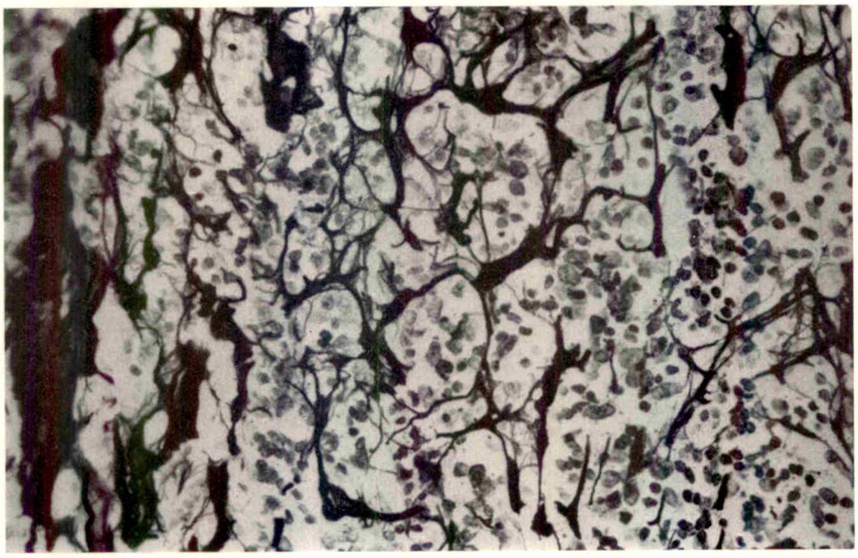

Fig. 3.

Photomicrograph of the tumour, showing groups of cells surrounded by fibrous septa to give a pseudoacinar or alveolar appearance.
(Gomori's silver impregnation, reticulin × 300)

The differential diagnosis of clear-cell sarcoma from synovial sarcoma has to be considered. Clinically the lack of pain during a major part of the long history favours clear-cell sarcoma, as does the site, antecedent trauma and slow growth with relentless multiple metastases. Histologically there was no evidence of the biphasic pattern seen in synovial sarcoma. There was a pseudoacinar alveolar arrangement in areas of the tumour and the PAS cytoplasmic granules were diastase sensitive, whereas they are diastase resistant in synovial sarcoma.

Our patient's tumour showed a remarkable sensitivity to both radiotherapy and chemotherapy. With regard to the latter a substantial mass of tumour completely regressed after only 2 mg of vincristine and 20 mg of bleomycin had been given.

Recent surveys of treatment for soft-tissue sarcomas (Chang, 1977; Wilbur *et al.*, 1975) have shown a wide variation in response to various agents and combinations including vincristine but there have been no reports for the combination of vincristine and bleomycin. As the suggested regimes for the chemotherapy of soft-tissue sarcomas are more unpleasant and associated with a greater morbidity than this combination, the marked sensitivity of this tumour to the combination of vincristine and bleomycin may therefore be of interest to other clinicians.

REFERENCES

Bearman, N. M., Now, J., and Kempson, R. L., 1975. Clear cell sarcoma with melanin pigment. *Cancer*, *36*, 977–984.

Bennett, G., 1947. Malignant neoplasms originating in synovial tissues (synoviomata). *Journal Bone Joint Surgery*, *29*, 259–291.

Chang, P., 1977. Management of soft tissue sarcomas. *American Journal of the Medical Sciences*, *273*, 244–257.

Dutra, F. W., 1970. Clear cell sarcoma of tendons and aponeuroses. *Cancer*, *25*, 942–946.

Enzinger, F. M., 1965. Clear cell sarcoma of tendons and aponeuroses. *Cancer*, *18*, 1163–1174.

Kubo, T., 1969. Clear cell sarcoma of patellar tendon studied by electron microscopy. *Cancer*, *24*, 948.

Mackenzie, D. H., 1974. Clear cell sarcoma of tendons and aponeuroses with melanin production. *Journal Pathology*, *114*, 231–232.

Samuel, M. L., Lanzotti, V. J., Holoye, P. Y., Boyle, L. E., Smith, T. L., and Johnson, D. E., 1976. Combination chemotherapy in germinal cell tumours. *Cancer Treatment Review*, *3*, 185–204.

Tsuneyoshi, M., 1975. Distinction of melanoma of soft parts from clear cell sarcoma of tendons and aponeuroses. *Fukuoka Acta Medica*, *66*, 666–681.

Wilbur, J. R., Sutow, W. W., Sullivan, M. P., and Gottlieb, J. A., 1975. Chemotherapy of sarcomas. *Cancer*, *36*, 765–679.

Book reviews

First year Physics for Radiographers. By George A. Hay and Donald Hughes, 1978, pp. xii+271 (Bailliere Tindall, London), £3·95.
ISBN 0–7020–0692–0.

In the preface to the second edition of their excellent book which covers the physics syllabus for the diploma of the College of Radiographers, Messrs Hay and Hughes describe minor modifications and additions that they have made, notably with respect to solid state rectifiers, and their emphasis on expressing X-ray spectra in terms of photon energy rather than wavelength.

The book is well laid out and in a similar style to the first edition, with many diagrams and with important points and laws emphasized in heavy type, a presentation which enables the student to use the book with ease.

Two minor criticisms would be: the continued use in places of conventional current flow, which, even allowing for the authors' prior warning, some students will still find confusing; and their proof of the inverse square law using similar triangles, where the radii of different spheres is more correct. But these are minor criticisms of what is a well written, readable book and remarkable value at £3·95. It is a book that most student radiographers will find invaluable in the preparation for their Part I examination.

R. S. Fairbanks.

Gastrointestinal Angiography. By S. R. Reuter and H. C. Redman, 1977, 2nd Edition, pp. ix+390, illus., (W. B. Saunders Co., Sussex), £20·00.

It is not uncommon to find oneself in difficulties to put major criticisms in polite words. It is very rare to experience difficulty in finding the right words in praise of an extraordinarily good text in radiology. This book falls into the latter category and is essential reading for all interested in abdominal angiography in any way.

I am a little surprised that the authors have not used subtraction techniques more widely which may make some of the illustrated points more clear for the uninitiated or inexperienced. Although the standard of the illustrations is excellent the book is not just an atlas but is accompanied by a very good text covering technique, equipment and normal anatomy in addition to the multitude of clinical examples. Each chapter is concluded with a full and worthwhile bibliography.

Too many words will dilute the praise. This is an excellent book.

A. B. Ayers.

1979, *British Journal of Radiology*, *52*, 242–243

Short communication

Carcinoma of the breast imaged by nuclear magnetic resonance (NMR)

By P. Mansfield, B.Sc., Ph.D., P. G. Morris, M.A., Ph.D., R. Ordidge, B.Sc.,

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(*Received October, 1978*)

NMR has shown promise as a non-invasive and non-hazardous method of imaging the mobile proton distribution (mainly water) on a small scale in both animal and human tissues (Mansfield and Maudsley, 1977) and more recently on a much larger whole-body scale (Mansfield, *et al.*, 1978; Damadian *et al.*, 1977).

In this paper we report the first localization of a breast cancer by this technique in a simple mastectomy specimen from a 47-year-old woman.

Following mastectomy the specimen was rapidly transferred from the City Hospital to the Physics Department and the NMR scan started about 1½ hours following operation. The specimen measured some 15 cm in the long axis, one end of which was the axillary tail; it had a maximum thickness of about 4 cm at the centre tapering off to about 1 cm at the periphery. The surface of the specimen was marked with waterproof ink for identification purposes and placed flat in a plastic container. The slice thickness scanned included the whole of the breast; the images produced correspond to coronal scan projections of water and fat distributed in the whole breast.

METHOD

The NMR line scanning technique used here has been largely described elsewhere (Mansfield, *et al.*, 1976). The principle of operation is: mobile protons contained in the water, fat or oil distributed throughout biological material are first aligned in a large static magnetic field. A weak nuclear magnetization results due to the small magnetic moment possessed by each proton or hydrogen nucleus. The weak polarization produced is proportional to the localized proton density (water content, etc.); this is read out line by line across the specimen by applying switched magnetic field gradients to define position within the specimen, and weak radiofrequency (rf) pulses tuned to the nuclear resonance frequency. The rf pulses perturb the nuclear magnetization from alignment and transient nuclear free-induction decay (FID) signals are recorded and Fourier analysed to yield the effective proton density of the specimen along a particular line.

The static field used was approximately 1 kG corresponding to a resonance frequency of 4.0 MHz.

In addition to distributed content of water and fat etc., the spatial distribution of spin lattice relaxation times T_1 (x, y) can be measured. T_1 is the time for disturbed protons to realign in the large polarizing field. Changes in T_1 reflect differences in mobility of the water and also differences in metabolic activity and dissolved salts contained in the cytoplasmic and extra-cellular water.

Immediately after scanning, the tissue was immersed in 20% formalin in which it remained for four days. It was then deep frozen and horizontal slices of about 8 mm thickness prepared and photographed. Paraffin sections of selected parts confirmed the presence of malignant tissue. The distribution of the carcinoma was reconstructed from the sections.

RESULTS AND DISCUSSION

The NMR images (Fig. 1A and B) reflect the general outline of the specimen. This correlates well with the outline of the fixed specimen (Fig. 2). In Fig. 1A each line of the picture was averaged 512 times with a delay of 0.15 sec. The dark zone to the right corresponds with the nipple region and underlying carcinoma and the larger dark central and left image corresponds to the main mass of the tumour (a scirrhous carcinoma). Bright zones on the scan correspond to normal breast tissue and the general gradation of the image intensity towards the periphery reflects the progressively reduced thickness of sample towards the edges. In normal tissue the thickest part of the specimen (the centre) would be expected to yield the brightest zone in the image.

Figure 1B is the same specimen scanned immediately after producing Fig 1A but with the delay time doubled to 0.3 sec. The dark nipple region remains but contrast in the tumourous region is reduced as a result of a somewhat longer T_1 compared with that of surrounding normal tissues (Damadian, 1971).

The image intensity of the nipple region does not change so significantly with decrease in repetition period and indicates that in the excized specimen this region has a lower water and/or fat content in keeping with known histological structures.

A second breast containing a large circumscribed fibroadenoma about 4 cm in diameter taken from a 73-year-old woman has also been examined and shows an image consistent with the tumour position.

Further study of breast tumours by NMR is continuing and we hope soon to be able to use the whole body imaging capability of the machine which allows examination of breasts *in vivo* before operation.

ACKNOWLEDGMENTS

We are grateful to the MRC for a project grant to support this work.

We are especially indebted to T. Baines for the design and construction of the electronic apparatus and V. Bangert for his assistance in the design of the gradient coils.

REFERENCES

DAMADIAN, R. 1971. Tumour detection by nuclear magnetic resonance. *Science, N.Y.*, *171*, 1151–1153.

DAMADIAN, R., GOLDSMITH, M. and MINKOFF, L. 1977. NMR in cancer: XVI. Fonar image of the live human body. *Physiological Chemistry and Physics*, *9*, 97.

MANSFIELD, P. and MAUDSLEY, A. A. 1977. Medical imaging by NMR. *British Journal of Radiology*, *50*, 188–194.

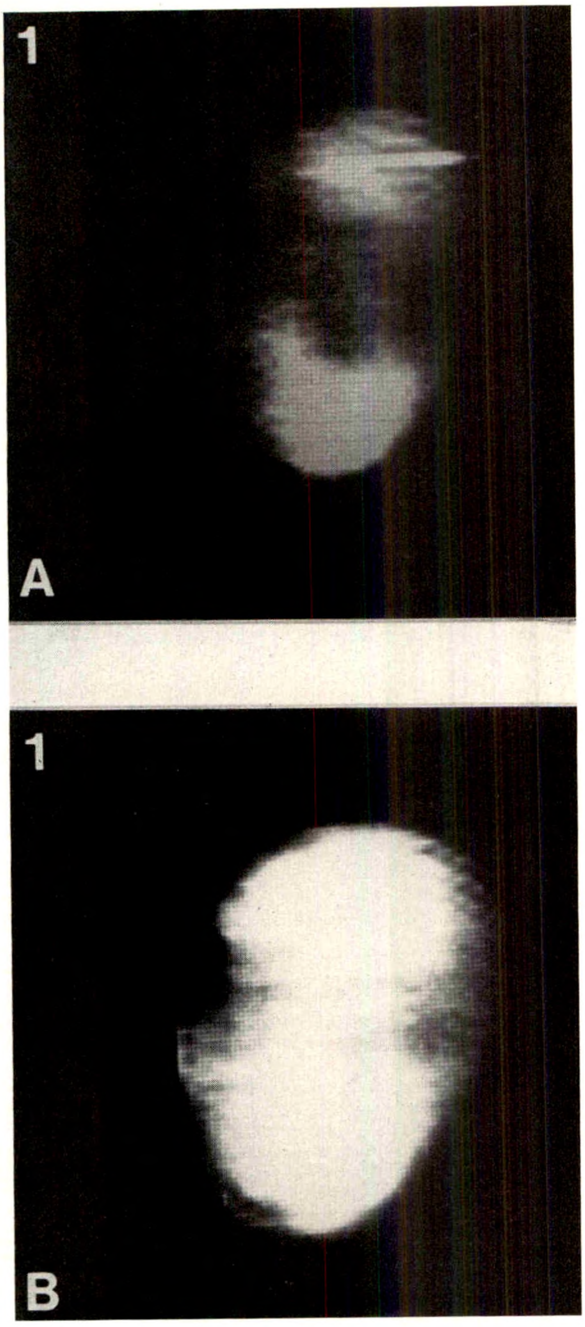

FIG. 1.

NMR line scan images of excised breast:
(A) Delay time 0.15 sec. Dark region to right corresponds with nipple. Dark central region corresponds to tumour site.
(B) Delay time is increased to 0.30 sec thus generally lowering picture contrast so that only the main mass of the tumour in the centre is revealed. Dark region to left of each picture corresponds to a notch in the tissue mass.

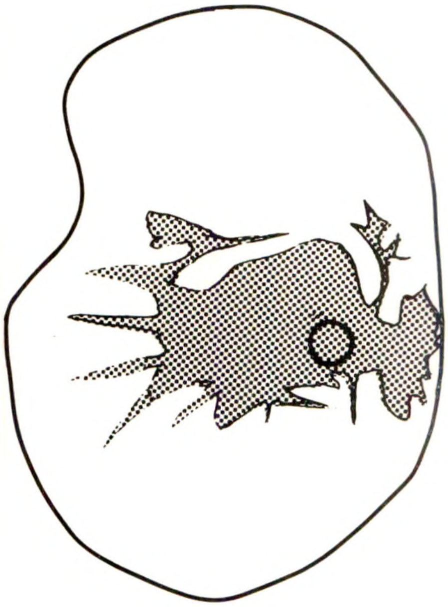

FIG. 2.

Reconstruction of position of scirrhous carcinoma which was thickest centrally and tapered towards left and right margins. Position of nipple indicated by black circle. Axillary tail is at the top of the specimen.

MANSFIELD, P., MAUDSLEY, A. A. and BAINES, T. 1976. Fast scan proton density imaging by NMR. *Journal of Physics, E*, *9*, 271–278.

MANSFIELD, P., PYKETT, I. L., MORRIS, P. G. and COUPLAND, R. E. 1978. Human whole body line scan imaging by NMR. *British Journal of Radiology*, *51*, 921–922.

1979, *British Journal of Radiology*, *52*, 244

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Anaesthesia and efficacy of hyperbaric oxygen in radiation therapy

THE EDITOR—SIR,

Respiration of pure oxygen at 200 kPa (two atmospheres) has been shown to be effective in achieving significant reductions in the TCD50 for fractionated radiation therapy of a number of experimental tumours (Suit and Maeda, 1967; Suite and Suchato, 1967, Suit *et al.*, 1977). This improvement in results was of large magnitude and was observed with all fractionation schedules where two or more fractions were employed. The ratio of TCD50 air/TCD50 O_2 at 200 kPa was in the range of 1.60–1.87 (Suit *et al.*, 1977). The effectiveness of hyperbaric oxygen with a single dose of radiation was much less impressive, viz. a ratio of 1.12 (Suit and Maeda, 1967). In all of these experiments the mice were anaesthetized with sodium pentobarbital (0.05 mg/g body weight). In the study discussed in this letter this ratio was much smaller in non-anaesthetized than in anaesthetized mice, viz. 1.23 *v.* 2.0.

Recently, a TCD50 assay at 200 kPa was performed with mice which were not anaesthetized. There was only a minimal reduction in TCD50 as compared with the control or air assay. After a careful review of that experimental protocol an experiment was designed to examine specifically the effect of pentobarbital anaesthesia to modify the response of our C3H mouse mammary carcinoma to O_2 at 200 kPa and radiation. Results of that experiment are shown in Table I. Third generation isotransplants of MDAH–MCaiv tumour were irradiated when 8 mm in diameter; radiation was given in two equal doses with 72 hours separation. The mice had been assigned by a random number scheme to one of the dose levels of one of three assays (A, B and C) at the time of transplantation. For the control assay (A), irradiation was performed under "air", normal breathing conditions without anaesthetic. In the test groups (B and C) tumours were irradiated while the mice respired O_2 at 200 kPa for 15 minutes before and then during each irradiation. Mice in Group B were unanaesthetized and those in Group C were given 0.05 mg/g body weight pentobarbital intraperitoneally before treatment. The TCD50 value for assay C is significantly lower that that for assay B ($p < 0.01$). The TCD50 for assay B is lower than that for assay A (air) ($p = 0.05$).

This large advantage given by anaesthesia in mice treated while respiring O_2 at 200 kPa is not due to any cytotoxic action of the pentobarbital. Earlier, TCD50 values were determined for air-breathing, normal or pentobarbital anaesthetized mice for radiation administered in ten equal doses with 24 hours between doses. The results were 10480 and 10400 rad respectively (Suit *et al.*, 1972). This finding is also not likely to be explained simply on the basis of the anaesthesia blocking the vaso-constriction induced by oxygen, as the ratio of TCD50 air/TCD50 O_2 200 kPa is only about 1.1 for single dose irradiation. Milne *et al.* (1973) have reported that for single dose irradiation of KHT sarcoma, respiration of O_2 at 200 kPa effected no greater reduction in survival fraction in control of pentobarbital treated hosts than for respiration of O_2 or air (Hill *et al.*, 1971) at normal pressure. We have experiments in progress which are designed to assist in elucidation of the mechanism of the phenomenon described in the murine tumour systems, with particular emphasis on fractionated irradiation.

The initial clinical experience with hyperbaric oxygen which was so optimistically interpreted was based on pentobarbital-anaesthetized patients (Churchill-Davidson *et al.*, 1955; 1957). However, virtually all subsequent work and the published reports of trials of hyperbaric oxygen are based on non-anaesthetized patients. From the data presented here the possibility of a role for anaesthesia in the clinical combination of hyperbaric oxygen and radiation therapy may be considered.

TABLE I

DEPENDENCE OF EFFICACY OF O_2 AT 200 KPA (2 ATMOSPHERES) TO REDUCE TCD50 AND USE OF ANAESTHESIA

Protocol MDAH–MCa IV 8 mm gkv = 2 $t_1 = 72$h $D_1 = D_2$		
Anaesthesia: Pentobarbital 0.05 mg/g body weight		
	TCD50 (95% Confidence limits)* rad	$\frac{\text{TCD50 air}}{\text{TCD50 } O_2}$
Air	7430 (6920 . . . 7980)	1.00
O_2 200 kPa No anaesthesia	6030 (5060 . . . 7180)	1.23
O_2 200 kPa Pentobarbital	3700 (2720 . . . 5040)	2.01

*Analysis on 120 day results.

Yours, etc.,

H. D. SUIT,
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(*Received September, 1978; revised November, 1978*)

REFERENCES

CHURCHILL-DAVIDSON, I., SANDER, C. and THOMLINSON, R. H., 1955. High-pressure oxygen and radiotherapy. *The Lancet*, 1091–1095.

1957. Oxygenation in radiotherapy. II. Clinical application. *British Journal of Radiology*, *30*, 406–422.

HILL, R. P., BUSH, R. S. and YEUNG, P., 1971. The effect of anaemia on the fraction of hypoxic cells in an experimental tumour. *British Journal of Radiology*, *44*, 299–304.

MILNE, N., HILL, R. P., BUSH, R. S., 1973. Factors affecting hypoxic KHT tumour cells in mice breathing O_2, $O_2 + CO_2$, or hyperbaric oxygen with or without anesthesia. *Radiology*, *106*, 663–671.

SUIT, H. D., HOWES, A. E. and HUNTER, N., 1977. Dependence of response of a C3H mammary carcinoma to fractionated irradiation on fractionation number and intertreatment interval. *Radiation Research*, *72*, 440–454.

SUIT, H. D. and MAEDA, M., 1967. Hyperbaric oxygen and radiobiology of a C3H mouse mammary carcinoma. *Journal of National Cancer Institute*, *39*, 639–652.

SUIT, H. D., MARSHALL, N. and WOERNER, D., 1972. Oxygen, oxygen plus carbon dioxide, and radiation therapy of a mouse mammary carcinoma. *Cancer*, *30*, 1154–1158.

SUIT, H. D. and SUCHATO, C., 1967. Hyperbaric oxygen and radiotherapy of a fibrosarcoma and of a squamous-cell carcinoma of C3H mice. *Radiology*, *89*, 713–719.

This work was supported by U.S. DHEW Grant CA13311.

Correspondence

Renography in the long-term follow-up of renal transplant patients

THE EDITOR—SIR,

The use of renography in the long-term follow-up of renal transplant patients as described by Doherty *et al.* (1978) is highly commendable. In their article the authors attach a great deal of importance to the shape characteristics of renogram curves as defined by the quantities: time to peak, second phase slope, sharpness of peak and rate of fall of third phase.

Despite the difficulties of interpreting these characteristics in a quantitative manner, they are always what one looks at when trying to make clinical judgements from renograms. Some of the uncertainties surrounding renogram shape characteristics can be reduced if the patient's urine flow-rate across the renogram is known.

Even when patients are not given any special instructions regarding hydration they can still arrive at the hospital in all conditions ranging from oliguric (*e.g.* 9.00 am appointment—no time for breakfast—no drink since last night) to highly diuretic (2.00 pm appointment—pub lunch plus two pints of beer across the road). The peak time of any renogram is strongly influenced by the urine flow-rate. In fact the whole shape of the curve can depend on this and a simple measurement of urine flow by emptying before and after renography helps enormously in the interpretation of bizarre shapes.

The normally smooth third phase of a renogram at urine flow-rates greater than 2 ml/min can become quite irregular at a urine flow of less than about 1.5 ml/min. Figure 3 in the article referred to shows a curve with a peak time of four minutes and an irregular descent phase and, as the author suggest, these irregularities could be due to abnormal peristalsis, variation in renal blood flow or vescico-ureteric reflux. It could also be a perfectly normal finding in the presence of a low urine flow-rate. The peak time of four minutes does suggest a urine flow-rate of 1.5 ml/min or less, a condition under which third phase irregularities are quite common and do not necessarily suggest abnormalities.

May we recommend that the standard renography protocol includes the measurement of urine flow rate—a measurement which we consider essential if the characteristics discussed are to have the clinical significance often accorded to them. Under some conditions oliguric and diuretic renograms can differ so markedly that one of them alone could not possibly tell the clinical story very satisfactorily. There is a case for suggesting that some patients should have, as standard procedure, two renograms at widely differing flow-rates.

Yours, etc.,
A. R. CONSTABLE,
S. ADLER,
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(*Received October, 1978*)

REFERENCE

DOHERTY, C. C., DOUGLAS, J. F., and MCGEOWN, MARY G., 1978. Isotope renography and long term follow-up of renal transplant patients. *British Journal of Radiology*, *51*, 802–807.

(*In reply*)

Renography in the long-term follow-up of renal transplant patients

THE EDITOR—SIR,

We endorse the recommendation of Dr. Constable and his colleagues (1979) that urine flow rate should be included in standard renography protocols, and omission of this information is a valid criticism of the methodology section of our paper (Doherty *et al.*, 1978). All renograms in the study were in fact carried out under conditions of diuresis, and therefore our observations on peak time and third phase irregularity cannot be attributed to low urine flow-rates as suggested. Our conclusions are therefore unchanged.

Yours, etc.,
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(*Received November, 1978*)

REFERENCES

CONSTABLE, A. R., ADLER, S., CRANAGE, R., and HOGBIN, E., 1979. Renography in the long-term follow-up of renal transplant patients. *British Journal of Radiology*, *52*, 245.

DOHERTY, C. C., DOUGLAS, J. F., and MCGEOWN, MARY G., 1978. Isotope renography and long-term follow-up of renal transplant patients. *British Journal of Radiology*, *51*, 802–807.

Book review

Guide pratique de Radiologie Vasculaire. By J. P. Monnier and J. Chermet, pp. viii+207, 1978 (Masson, Paris), F.80. ISBN 2-225-49335-9.

This small French monograph sets out to provide a practical guide to vascular radiology. After a preliminary section on technique, materials, anaesthetics, and general supervision, various types of arteriography are considered in detail. It lists most vascular investigations and provides brief technical information as to the method of carrying them out. There are some 20 illustrations in the form of diagrams, but no X-ray reproductions.

This is not a book to recommend to beginners in angiography since your reviewer believes that angiography is a technique in which proficiency and safety can only be learnt at first hand by practical instruction on the apprentice system. However, the book could prove useful to experienced workers in angiography who wished to check up on points of detail about particular procedures.

D. SUTTON.

1979, *British Journal of Radiology*, *52*, 246–252

Proceedings of The British Institute of Radiology

Benign bone disease—role of radioisotope techniques

Abstracts of papers presented at a combined meeting of The British Institute of Radiology and the British Orthopaedic Association on Wednesday, May 31, 1978, at the Edward Lewis Theatre, The Middlesex Hospital Medical School, Mortimer Street, London, W.1.

The mechanism of uptake of ^{99}Tc^{m}-labelled phosphates, by J. P. Lavender.
Bone scintigraphy in the early diagnosis of caisson disease of bone—an experimental study, by P. J. Gregg, J. Stothard and D. N. Walder.
A quantitative assessment of femoral head activity using ^{99}Tc^{m}-labelled phosphates and a computer data collecting system, by T. R. Morley, D. J. Dowsett and M. D. Short.
The bone scan in acromegaly, by I. Fogelman, I. D. Hay, J. G. Turner, D. H. Carr, D. L. Citrin and W. R. Greig.
The diagnostic role of bone scanning in paediatrics, by J. M. Ash.
Evaluation of therapy in Paget's disease by means of bone scintigraphy, by C. J. L. R. Vellenga, E. K. J. Pauwels, O. L. M. Bijvoet and W. B. Frijlink.
The use of ^{99}Tc^{m}-diphosphonate in the evaluation of metabolic bone disease, by I. Fogelman, J. G. Turner, D. L. Citrin, I. T. Boyle and W. R. Greig.
The use of radioisotope imaging in the diagnosis of stress and scaphoid fractures, by A. J. W. Hilson, T. F. El Sayed, A. J. S. Saunders and M. N. Maisey.
The value of bone scanning in the early diagnosis of osteoid osteoma, by D. C. Jameson Evans and D. L. Gilday.
Scintigraphy in the early diagnosis of sacro-ileitis, by E. C. Dunn, R. W. Ebringer and P. J. Ell.
The bone scan as an aid to therapy in paediatric disease, by J. M. Ash.
An experimental model of disc space infection and its early diagnosis by Ga scanning, by S. H. Norris, M. G. Ehrlich and K. McKusick.
Scintigraphic and roentgenographic evaluation of total hip endoprostheses, by W. Bessler.
^{99}Tc^{m} methylene diphosphonate scanning in Thompson hemiarthroplasties, by N. Rushton and E. P. Wraight.
Bone scintigraphy in dialysis patients, by P. de Graaf and E. K. J. Pauwels.
Bone densitometry in renal patients, by E. G. A. Aird, T. G. Feest and D. N. S. Kerr.
An intravenous radioisotope technique for the diagnosis of synovial rupture of the knee, by D. Ottewell, Anne Woodford and R. W. Porter.
Quantitation of ^{99}Tc^{m}-phosphate uptake by emission tomography, by P. H. Jarritt and P. J. Ell.

THE MECHANISM OF UPTAKE OF ^{99}Tc^{m} LABELLED PHOSPHATES

By J. P. Lavender

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The mechanism of the uptake of radionuclides into bone has been the subject of discussion over a number of years. The two general mechanisms that can be postulated would be that of the regional distribution of bone blood flow or alternatively a change in the extraction efficiency of bone.

We have used several experimental approaches to this problem all based on a model involving the injection of a bone-seeking radionuclide (technetium labelled methylene diphosphonate—^{99}Tc^{m}-MDP) into the nutrient artery of the tibia of the dog. The first sequence of experiments was to look at the immediate extraction and four hour residue in normal and abnormal bone. It was found that although the immediate extraction into bone was fairly high the radioactivity was washed out from bone and left a four hour residue in normal bone of 4.9±1%. In abnormal bone, however, this residue was increased 13.4±1.1%.

The second approach was to compare the regional distribution of the bone-seeking isotope with the regional distribution of blood flow to the bone. Profiles of blood flow were produced by injecting labelled radioactive microspheres into the nutrient artery and also by observing the steady state radioactivity produced by a constant infusion of the short-lived gas krypton 81m. Profiles of the distribution of the bone-seeking isotope differed from the profiles of regional blood distribution both in normal and abnormal bone and showed that for moderate increases in flow associated with a fractured bone there was a marked increase in radionuclide uptake.

Lastly, autoradiographs of rat bone were performed both following an intravenous bolus and following incubation of bone with the bone-seeking isotope ^{99}Tc^{m}-MDP. Both autoradiographs showed increases of activity in the region of newly-formed bone adjacent to the epiphyseal plate. This technique therefore demonstrates that uptake of radioisotope into bone is not uniform but is increased in newly formed bone even *in vitro*.

In conclusion, therefore, we would suggest that the distribution of bone-seeking isotopes is dependent on bone blood flow but also on a local factor causing an increase in "avidity".

BONE SCINTIGRAPHY IN THE EARLY DIAGNOSIS OF CAISSON DISEASE OF BONE—AN EXPERIMENTAL STUDY

By P. J. Gregg, J. Stothard and D. N. Walder

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Caisson disease of bone affects compressed air workers and divers (McCallum, 1975) and is characterized by the presence of bone and marrow necrosis which may result in the development of a severe arthrosis of both shoulders and hips. Prevention is not possible, treatment unsatisfactory and therefore early diagnosis is important in order that an affected individual may be advised to stop this type of work

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before the condition reaches an advanced state. Radiography is unsatisfactory (Davidson, 1976) because of the long delay between the causal incident and the appearance of an abnormality. Whether bone scintigraphy could detect the new bone formation known to be present in an affected area at an early stage has been investigated.

Bone and marrow necrosis was produced by embolism of rabbit femora with glass microspheres. It was possible to detect areas of bone/marrow necrosis (as "hot-spots" three weeks after operation by ^{99}Tc^{m}-diphosphonate scintigraphy whereas radiographs remained normal for 12 weeks. Histological examination of excised femora confirmed the presence of bone necrosis associated with new bone formation in the abnormal areas depicted on the scintigram. In addition there were also areas of bone necrosis, not associated with new bone formation, which were not detected on the scintigram. New bone formation was present not only in relation to dead bone but also in dead marrow.

Preliminary use of scintigraphy in North Sea divers has shown that this may be a useful method for surveillance of this group of men.

REFERENCES

McCALLUM, R. I., 1975. Dysbaric osteonecrosis: aseptic necrosis of bone. In *The Physiology and Medicine of Diving and Compressed Air Work*, edited by P. B. Bennett and D. H. Elliott, pp. 504–521 (London, Bailliere Tindall).

DAVIDSON, J. K., 1976. Dysbaric osteonecrosis. In *Aseptic Necrosis of Bone*, edited by J. K. Davidson, pp. 147–212 (Amsterdam, Excerpta Medica).

A QUANTITATIVE ASSESSMENT OF FEMORAL HEAD ACTIVITY USING ^{99}Tc^{m}-LABELLED PHOSPHATES AND A COMPUTER DATA COLLECTING SYSTEM

By T. R. Morley

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D. J. Dowsett and M. D. Short

Department of Medical Physics and Bio-Engineering University College Hospital, Gower Street, London WC1

A technique was described for assessing the abnormal femoral head activity in Legg-Calve-Perthes' disease, using ^{99}Tc^{m}-labelled phosphates. Thirty-six children, between the ages of 4 and 11, with either confirmed or suspected Perthes' disease, were investigated and a control group of 28 children scanned for other pathology was used. All the children were scanned on an out-patient basis. Following intravenous injection of the isotope, the child was placed supine under a gamma camera and a total of 500,000 counts was collected, by a computer, using a high sensitivity, low energy, parallel hole collimator. A reference point on the data matrix which was unaffected by the disease, was used for deriving comparative uptake ratios in each femoral head. This reference point remained unaltered during surgical procedure or during the follow-up period. The use of the technique was discussed in early diagnosis and follow up, both in unilateral and bilateral disease.

THE BONE SCAN IN ACROMEGALY

By I. Fogelman, I. D. Hay, J. G. Turner, D. H. Carr, D. L. Citrin and W. R. Greig

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Technetium-99m diphosphonate bone scans were performed in 20 acromegalic patients. Twelve patients had active disease with elevated basal human growth hormone (HGH) levels. Eight patients were in clinical and biochemical remission.

The bone scans were assessed independently by three observers for features considered characteristic of increased metabolic bone activity, *i.e.* increased tracer uptake by axial skeleton, long bones and wrists; prominence of calvarium and mandible; beading of the costo-chondral junctions; a "tie" sternum; and faint or absent kidney images. These scan features were numerically graded and the total score for each patient defined as the "metabolic index".

The metabolic index correlated well with biochemical activity as measured by HGH radioimmunoassay ($R = 0.72$; $p < 0.001$) and accurately identified those patients with severely active disease (HGH > 50 mU/l).

It is considered that the bone scan and derived metabolic index may provide a means of assessing current metabolic activity in patients with acromegaly. This may be of value in the post-operative period when HGH may not be an accurate measure, or where there is a discrepancy between clinical assessment and biochemical findings.

THE DIAGNOSTIC ROLE OF BONE SCANNING IN PAEDIATRICS

By J. M. Ash

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Bone scanning using ^{99}Tc^{m}-phosphate compounds has become an important diagnostic tool in benign paediatric bone disease, both to diagnose unspecified bone pain and to rule out malignancy in known lesions.

It is useful to characterize and define bone abnormalities which may or may not be present radiologically. The study should include "blood pool" images of appropriate sites performed immediately after injection, as well as delayed scans to gain optimum information regarding the nature of the lesion.

In contrast to malignant tumours, most benign neoplasms will show either no abnormal uptake or slightly increased radioactivity, *e.g.* fibrous cortical defect, benign cyst, osteochondroma (Gilday and Ash, 1976). In this way malignancy may be ruled out, although occasionally an osteochondroma can show marked increased uptake without malignant change. Typically an aneurysmal bone cyst will show increased vascularity on the blood pool image with uptake at its margin on the delayed scan. Osteoid osteoma may be difficult to see radiologically, particularly in the spine, but shows marked focal accumulation on the bone scan. In 19 cases, all look typically positive scans of which two were not seen radiologically and three were seen only in retrospect.

Occult bone trauma is readily detected particularly in the battered child and vascularity may be assessed where bone necrosis is suspected.

Osteomyelitis may be differentiated from cellulitis by the more focal increase in bone activity on both the blood pool and delayed images. The scan is frequently positive before radiographic changes are present, and so is useful in detecting infection, particularly in unusual sites and in discitis. Absent radioactivity is seen if septic necrosis has occurred. In 43 patients with normal scans, only one had osteomyelitis and one septic arthritis. Seventy out of 70 cases of osteomyelitis were correctly diagnosed as were 13 out of 13 cases of cellulitis and eight out of eight cases of septic arthritis (Gilday *et al.*, 1975). However, only four out of 14 sites of involvement were detected in neonates with osteomyelitis even using magnification and high resolution techniques. Many of these patients had marked radiographic bone changes. Gallium-67 citrate may be useful in equivocal cases.

When the radiographs are normal or equivocal the bone scan may be used as an aid to diagnosis and also to direct further X-ray investigation; when radiographs are abnormal the bone scan can be useful to characterize the lesion.

REFERENCES

Gilday, D. L., and Ash, J. M., 1976. Benign bone tumours. *Seminars in Nuclear Medicine*, *6*, 33–46.

Gilday, D. L., Paul, D. J., and Patterson, J., 1975. Diagnosis of osteomyelitis in children by combined blood pool and bone imaging. *Radiology*, *117*, 331–335.

EVALUATION OF THERAPY IN PAGET'S DISEASE BY MEANS OF BONE SCINTIGRAPHY

By C. J. L. R. Vellenga, E. K. J. Pauwels, O. L. M. Bijvoet and W. B. Frijlink

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In a previous publication the merits of bone scintigraphy in Paget's disease were stressed (Vellenga *et al.*, 1976). In this study the value of bone-scintigraphy in the evaluation of the therapeutic effect of a combination of calcitonin and EHDP was determined. Thirty patients were studied half-yearly using 20 mCi ^{99}Tc^{m}-EHDP and a scoring method ranging from 1 to 6 (1 = normal, 6 = extremely abnormal). The skull tended to get highest scores, the spine lowest scores. Monostotic lesions showed higher scores and did not normalize.

Although of these 30 patients 25 normalized biochemically (Bijvoet *et al.*, 1979), only two did so scintigraphically. Of 106 affected bones only 36 normalized.

Moreover, ten patients deteriorated; seven during treatment and three after the end of treatment. This deterioration was confirmed biochemically in five patients, usually several months after scintigraphic deterioration. With higher initial scores, tendency to later deterioration is greater.

Conclusions:

(1) There are different "Paget's diseases", depending on the site in the skeleton. Initial activity, response to therapy and behaviour after stopping therapy are not equal.

(2) Normalization of biochemical values does not implicate normalization of local disease.

(3) Bone scintigraphy might be the most sensitive parameter for the activity of the disease and will detect deterioration earlier than biochemistry does.

(4) There still are many unsolved questions on the mechanism of uptake of scintigraphic agents and results therefore should be interpreted carefully.

REFERENCES

Vellenga, C. J. L. R., Pauwels, E. K. J., Bijvoet, O. L. M. and Hosking, D. J., 1976. Evaluation of scintigraphic and roentgenologic studies in Paget's disease under treatment. *Radiologica Clinica*, *45*, 292–301.

Bijvoet, O. L. M., Hosking, D. J. Frijlink, W. B., Te Velde, J., Vellenga, C. J. L. R., and Pauwels, E. K. J., 1979. Treatment of Paget's disease with combined calcitonin and diphosphonate. *Metabolic Bone Disease and Related Research* (in press).

THE USE OF ^{99}Tc^{m}-DIPHOSPHONATE IN THE EVALUATION OF METABOLIC BONE DISEASE

By I. Fogelman, J. G. Turner, D. L. Citrin, I. T. Boyle and W. R. Greig

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It is now apparent that recognizable patterns of abnormality and several "metabolic features" may be seen on the bone scans of patients with metabolic bone disease (Fogelman *et al.*, 1978). However, skeletal imaging is of limited value in the diagnosis and evaluation of those patients providing the most difficulty in clinical practice, *e.g.* patients with osteoporosis or "mild" primary hyperparathyroidism. In such cases quantitation of skeletal uptake of radiopharmaceutical may be of value.

Skeletal avidity for ^{99}Tc^{m}-hydroxyethylidene diphosphonate (HEDP) is related to bone blood flow and osteoblastic activity and there is rapid renal excretion of administered activity not taken up by bone. We have, therefore, suggested that 24 hour whole body retention of ^{99}Tc^{m}-HEDP may be an accurate index of bone metabolism, both in health and disease.

Using a shadow-shield whole-body monitor we have measured 24 hour skeletal uptake of ^{99}Tc^{m}-HEDP in 68 healthy control subjects and 77 patients with metabolic bone disease. The renal osteodystrophy, Paget's, osteomalacia and primary hyperparathyroidism groups had significantly elevated values for ^{99}Tc^{m}-HEDP retention ($p < 0.001$) and each individual result in these groups lay outside the control range. The osteoporotic group could also be distinguished from the control population ($p < 0.001$) but some individual results were normal.

It is concluded that 24 hour skeletel uptake of ^{99}Tc^{m}-HEDP provides useful supplementary information to the bone scan and is a sensitive indicator of conditions with increased bone turnover.

REFERENCE

Fogelman, I., McKillop, J. H., Bessent, R. G., Boyle, I. T., Turner, J. G., and Greig, W. R., 1978. The role of bone scanning in osteomalacia. *Journal of Nuclear Medicine*, *18*, 245–248.

THE USE OF RADIOISOTOPE IMAGING IN THE DIAGNOSIS OF STRESS AND SCAPHOID FRACTURES

By A. J. W. Hilson, T. F. El Sayed, A. J. S. Saunders and M. N. Maisey

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In view of the previously reported use of bone imaging in military stress fractures, we have performed a series of studies in 18 athletes and ballet dancers with suspected stress fractures and also in eight patients with suspected scaphoid fractures. In all cases the results were compared with the radiographic findings.

In all cases of suspected stress fracture where the X rays and nuclear medicine study were performed at the same time, the radioisotope study showed a higher sensitivity and was positive in 15 out of 18 patients. In particular, the nuclear medicine study often showed multiple lesions where only one was visible radiologically, and it was also of value in assessing progress.

In 17 patients with suspected scaphoid fractures, with X rays which were negative at the time of visit to the casualty department, six had focally positive scans, of which four were later positive on X ray.

Our findings would suggest that radioisotope scan is the initial investigation of choice in patients with suspected stress fracture, particularly as a correct diagnosis allows early return to training if negative. The place of imaging in suspected scaphoid fracture is less clear, and further studies are being performed.

THE VALUE OF BONE SCANNING IN THE EARLY DIAGNOSIS OF OSTEOID OSTEOMA

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The efficiency of diagnosis of osteoid osteoma is compared before and after the introduction of bone scanning. Osteoid osteoma may lie latent to radiographic diagnosis and when manifest may be poorly localized. Scans were performed using ^{99}Tc^{m}-methylene diphosphonate. Twenty-seven cases were reviewed, 17 diagnosed prior to the introduction of scanning and ten after. Before the introduction of scanning, the average delay in diagnosis from presentation was 10.5 months whereas it was immediate where scanning was employed. In the unscanned group, additional investigations included five myelograms, one arteriogram and three psychiatric referrals. One child was subjected to laminectomy without improvement. In addition six cases required re-operation for recurrence. In the scanned group, no highly invasive investigations were employed and no recurrences have yet been reported, the minimum follow-up being two years. Bone scanning has proved to be useful in accurate localization of the lesion resulting in complete removal. This has been particularly helpful in the spine where radiographic localization may be lacking. The appearances on the scan of osteoid osteoma are characterized by a small area of high uptake.

It is felt that bone scanning should be employed early in children with unexplained bone pain.

SCINTIGRAPHY IN THE EARLY DIAGNOSIS OF SACRO-ILEITIS

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PURPOSE

The aim of the study was to establish the usefulness of a quantitative technique for measuring the uptake of ^{99}Tc^{m}-labelled phosphates in the skeleton as a method of detecting inflammatory change in suspected early sacro-ileitis. This condition is difficult to diagnose in the early stages, since radiological changes appear late, and serum enzyme methods are non-specific.

METHOD

For this purpose, a large field Nuclear Enterprises Digicamera with a 32K store general purposes computer was used. Patients were imaged after intravenous administration of 15 mCi of ^{99}Tc^{m}-MDP (methylene diphosphonate). Routine 400K count images were recorded of the posterior pelvis, SI joints and lumbar spine. Fractional quantitation was performed by dividing the sacroiliac region into three horizontal, adjacent, but non-overlapping areas, and counts were taken over both sacroiliac joints and central sacrum at each level. After background subtraction, sacroiliac/sacral ratios and a sacroiliac index were calculated for each subject (Russell *et al.*, 1975; McIntyre *et al.*, 1977). A total of 31 bone scans have been performed to date in subjects under 45 years, including six normal controls, five patients with clinically definite active ankylosing spondylitis, two Reiter's disease and two with psoriasis and 16 patients with low back pain, and possibly early sacro-ileitis.

RESULTS

Bilaterally high uptake giving high SI/S ratio and high S-I index were obtained in four patients with AS and six of the group with suspected sacro-ileitis. Unilateral high uptake and high SI/S ratio were obtained in three subjects (two Reiter's syndrome, one psoriasis). All these had grade 0–2 sacroiliac X rays (normal to minimal change). Two AS patients with grade three X rays (definite change) had SI/S ratios and SI index within the normal range.

CONCLUSION

The data shows that quantitative scintigraphy is useful in the early diagnosis of sacro-ileitis (prior to definite X-ray changes). It is not useful to apply the technique once definite X-ray changes are established. For sensitive detection, each S-I joint requires multi-level analysis. The procedure is particularly useful for monitoring during follow-up.

REFERENCES

RUSSELL, A. S., LEUTE, B. C., and PERCY, J. S., 1975. Investigation of sacroiliac disease: comparative evaluation of radiological and radionuclide techniques. *Journal of Rheumatology*, *2*, 45–51.

NANCY, T. C., MCINTYRE, J., BUSE, MARIA, and LEROY, E. C., 1977. Nucleargraphic studies in axial spondarthritides. 1. Quantitative sacroiliac scintigraphy in early HLA B27 associated sacro-ileitis. *Arthritis and Rheumatism*, *20*, 5.

THE BONE SCAN AS AN AID TO THERAPY IN PAEDIATRIC DISEASE

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Bone scanning is useful to assess the response to therapy in certain diseases as well as to indicate the stage of the disease, particularly in the hip.

After the injection of a ^{99}Tc^{m}-phosphate compound the hip is imaged in internal rotation, using routine gamma camera and pinhole magnification (2.3 mm insert) techniques. An image of the affected hip is taken for the same time as the normal one, so that one can compare the relative activity (Ash *et al.*, 1975). Approximately two-thirds of the children presenting with symptomatic hips were studied for synovitis or Legg-Perthes disease. One hundred and five scans were done for suspected synovitis or Legg-Perthes; seven showed decreased activity in the femoral head (five had normal and two had equivocal radiographs). Thirty-six patients with Legg-Perthes were studied to stage the disease. Patients with synovitis will show either normal uptake or slight diffuse increase over the affected hip; none with this appearance later developed Legg-Perthes disease. Those with Legg-Perthes show either partial or total absence of activity in the femoral head initially. When revascularization occurs, a band of increased activity is seen laterally in the head. Since the bone scan abnormalities antedate the radiographic changes by several months, it is useful in initiating appropriate management (Danigelis, 1976).

Decreased activity in the femoral head in patients with joint effusions indicates ischaemia and the need for immediate aspiration if necrosis is to be avoided. Following a fracture of the femoral neck or a slipped femoral capital epiphysis, the scan is valuable in assessing viability of the femoral head. Serial studies are subsequently performed to monitor healing after pinning and to show fusion of the epiphyseal plates before removal of the pins.

In children with arthritidees, the bone scan can be used to detect sub-clinical involvement of joints, especially on the blood pool image, and to assess the response to therapy. The bone scan is of potential value to demonstrate pseudarthroses as a cause of back pain in patients with scoliosis treated surgically, and to indicate the metabolic activity of soft tissue ossification in cases of myositis ossificans, being considered for surgery.

Fusing cranial sutures initially show increased activity on the bone scan and later decreased activity when the process is complete. False positives may occur if one is not aware of reactive increases in normal sutures; lambdoid sutures are difficult to assess in a very young infant and may give false negative results. When the radiographs are equivocal in craniosynostosis, the bone scan is valuable in deciding which sutures are involved (Tait *et al.*, 1979).

REFERENCES

ASH, J. M., GILDAY, D. L., and REILLY, B. J., 1975. Pinhole imaging of hips disorders in children. Abstract. *Journal of Nuclear Medicine*, *16*, 512–513.

DANIGELIS, J. A., 1976. Pinhole imaging in Legg-Perthes disease; further observations. *Seminars in Nuclear Medicine*, *6*, 69–82.

TAIT, M. V., GILDAY, D. L., ASH, J. M., BOLDT, A. J., HARWOOD-NASH, D. C. F., FITZ, C. R., and BERRY, J., 1979. Craniosynostosis—correlation of bone scans, radiographs and surgery. *Radiology* (in press).

AN EXPERIMENTAL MODEL OF DISC SPACE INFECTION AND ITS EARLY DIAGNOSIS BY Ga SCANNING

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The authors stated that the pathogenesis of disc space infection is unknown. Some authors believe the disease to start primarily in the intervertebral disc and others believe that the infection commences primarily in the vertebral body and invades the disc as a secondary event. By creating an experimental model of disc infection in rabbits by inoculating the disc with staphylococci under direct vision, they showed that the infection does commence primarily in the intervertebral disc. In addition the authors have confirmed a clinical finding which suggested that the diagnosis may be made earlier with ^{67}Ga-citrate as an isotope than ^{99}Tc^{m}-diphosphonate. Using two groups of animals, one scanned *in vivo* and the other scanned *in vitro* it was shown that ^{67}Ga scan becomes positive within 24 hours and that at about three weeks the ^{99}Tc^{m} scan is positive which is about the same time that the radiographs show signs of infection. It is suggested on the basis of this experiment that ^{67}Ga be used as the isotope of choice in the diagnosis of this disease in the clinical context.

SCINTIGRAPHIC AND ROENTGENOGRAPHIC EVALUATION OF TOTAL HIP ENDOPROSTHESES

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Roentgenograms and scintigrams of 78 hip endoprostheses were assessed by comparative examinations. A loosening of the acetabular cup was present in seven hips and a loosening of the femoral stem in 34 hips. An infection had occurred in two cases with stable and in nine cases with unstable hip endoprostheses. As symptoms of a loosening of a prosthetic component signs of bone resorption, cortical erosions, cracks in the bone cement and a change of the position were observed on roentgenograms and a focal or diffuse increase of the tracer uptake on the scintigrams. Corresponding roentgenographic and scintigraphic findings were seen in 12 stable and in 31 unstable hips. Twenty-five acetabular cups and eight femoral stems showed symptoms of loosening on the roentgenogram, but in fact were stable as could be proven by the scintigram and the further clinical course or by re-operation. The loosening of the femoral prosthetic components with negative roentgenograms was demonstrated by bone scans in six cases. In hips with a rigid seat of the arthroplasty an increased tracer uptake was seen in recently implanted prostheses or was caused by resorptive bone processes, by abnormal pressure effects on bone, by soft tissue calcifications or by pseudoarthrosis of the major trochanter. In the assessment of hip endoprostheses minor details on the roentgenograms have to be noted and compared with the scintigraphic findings. For the interpretation of the scintigram the exact localization of an increased tracer uptake has to be found out by comparison with the respective roentgenogram. In special cases of hip endoprostheses causing discomfort to the patient, which cannot be clarified by the clinical and the roentgenographical examinations, bone scanning can be of value.

^{99}Tc^{m}-METHYLENE DIPHOSPHONATE SCANNING IN THOMPSON HEMIARTHROPLASTIES

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All patients considered had had a Thompson hemiarthroplasty for fractured neck of femur, all were well, mobile, and had no significant hip symptoms. Clinical and haematological examinations were used to exclude infection.

The patients were divided into loose or firmly fixed (control) groups according to radiological evidence (some prostheses were not fixed with bone cement). The average time from arthroplasty to scan with 15 mCi ^{99}Tc^{m} methylene diphosphonate was 18 months. Five out of six patients with loose prostheses showed focal increase around the prosthesis. One patient showed significant but diffuse increase. The eight patients of the control group showed either minimal diffuse uptake or no increase.

The indication of loosening was felt to be focal increase in uptake particularly in the areas around the hip and collar of the prosthesis.

The acetabular area was studied and either diffuse uptake or no increase was determined.

The time from arthroplasty to scan was considered and it was concluded that around a femoral prosthesis a minimum of ten months is needed before the final post-operative level is reached.

BONE SCINTIGRAPHY IN DIALYSIS PATIENTS

By P. de Graaf and E. K. J. Pauwels

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The value of ^{99}Tc^{m}-EHDP scintigraphy in the detection of renal osteodystrophy and metastatic pulmonary calcification was studied in 30 dialysis patients, after reducing background activity with haemodialysis to levels found in a normal control group. Scans were obtained after 6 hours and quantitative data were collected by registering count rates in standardized regions of interest in both groups.

All patients had histological evidence of renal osteodystrophy, but only 46% showed X-ray abnormalities. However, abnormal scans were found in 83% and quantitative analysis showed increased skeletal activity accumulation in all patients, when compared with normals. Bone scintigraphy thus appears to be a sensitive method for detecting skeletal involvement in renal osteodystrophy (de Graaf *et al.*, 1979).

Pulmonary calcification, which occurs in dialysis patients, is known from autopsy studies to have an incidence of about 60–70%, was detected with scintigraphy only in one patient and histological proof of extensive calcification was obtained. High chest-to-spine activity ratios were found in 66% of the patients, when compared with normals, and was highest in the patient with proven calcification. Although these high ratios are suggestive for increased pulmonary radionuclide uptake, conclusive evidence could not be obtained in the remaining patients. Hence, it appears that bone scintigraphy is not a sensitive method for detecting uraemic pulmonary calcification, with the exception of severe calcification. This is probably due to the fact that uraemic pulmonary calcification is not crystalline apatite, but a more amorphous compound (Conger and Alfrey, 1976).

REFERENCES

De Graaf, P., Schicht, I. M., Pauwels, E. K. J., Te Velde, J., and De Graeff, J., 1979. Bone scintigraphy in renal osteodystrophy. *Journal of Nuclear Medicine* (in press).

Conger, J. D., and Alfrey, A. C., 1976. In comment: scanning for pulmonary calcification. *Annals of Internal Medicine, 84*, 224–225.

BONE DENSITOMETRY IN RENAL PATIENTS

By E. G. A. Aird

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Renal osteodystrophy has many components, including osteitis fibrosa, osteomalacia, osteoporosis, and osteosclerosis. The disease pattern changes during transition from chronic renal failure to dialysis to transplant, and at times is severe and incapacitating. Traditional assessment by clinical, biochemical and radiological techniques has failed to detect small changes in bone, and bone biopsy is too invasive for regular repeated use. In a search for an accurate non-invasive technique of assessing changes in bone, we have used serial photon absorptiometry (PA) to measure bone mineral content in 200 patients with renal failure.

Samarium, which is virtually monochromatic, quantum energy of 42 KeV, was used as an X-ray source. Bone mineral content (BMC) in g/cm was computed from the differential absorption of the X rays by bone and surrounding tissues, using the results of two parallel scans 1 cm apart over the lower femur. The reproducibility of this technique gave a standard deviation of 4.5%. Patients were studied at one to two monthly intervals and the significance of changes was tested using either the method of least squares, or by taking the means of two separate periods of six months in an individual patient, and comparing them using student's "t" test. We performed studies on 17 male and 14 female normal controls, 80 patients on haemodialysis for periods varying from one to four years, 36 patients from the time of renal transplant, and 40 late post-transplant patients.

In all groups the BMC of women was significantly less than in men and absolute values of BMC were reduced compared with controls in both dialysis and transplant patients. Serial observations showed that at least 50% of patients significantly lose bone mineral during the first year of dialysis and no patients gain. This loss appears to diminish in subsequent years. Of 21 dialysis patients treated with 1α vitamin D_3, only one lost bone mineral and nine showed significant gains during the first year of treatment: these gains were more marked in females, and diminished during the second year of treatment, although BMC was still below the normal range. Following renal transplant, men and young women showed a tendency to lose a small amount of BMC during the first year after transplantation but post-menopausal women showed marked losses of BMC during this period. Studies on patients who had had transplants for more than three years showed 15% had an overall gain of bone mineral each year, 8% a loss and 77% were static. This suggests that the loss of mineral following transplant ceases within two to three years, and may be related to the high dose of steroids given during the first year following operation.

Interpretation of these results is difficult, as measurement of BMC gives no indication of underlying histological changes in the bones, and as yet photon absorptiometry is not of use in making routine clinical decisions. As more information accumulates it may be possible to correlate changes in BMC with histological changes in dialysis patients. At present PA is most likely to be of use in following transplant patients, in whom osteomalacia and osteitis fibrosa are known to heal: osteoporosis is known to occur, but is extremely difficult to measure radiologically or histologically, and serial measurement of BMC may therefore be a very useful way of studying this, and of identifying groups of patients at greatest risk of developing osteoporosis. Serial measurement of BMC also appears to be a useful research tool for measuring changes in bone during therapeutic trials.

AN INTRAVENOUS RADIOISOTOPE TECHNIQUE FOR THE DIAGNOSIS OF SYNOVIAL RUPTURE OF THE KNEE

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Rupture of the synovium of the knee may result in synovial fluid entering the deep tissues of the calf, and as the associated symptoms are also characteristic of a deep venous thrombosis, it is important to distinguish between the two.

Techniques involving intra-articular injections of radio-opaque or radioactive material into the knee-joint have been used in the diagnosis of synovial rupture, but neither is without pain or complications. The use of a radioactive tracer, injected intravenously, is presented as a simple, safe and reliable method of diagnostic confirmation.

The radioactive tracer media were selected from a group established in the field of skeletal imaging, as it has been determined that these long-chained molecules become trapped in synovial fluid before being absorbed by bone. One hour after injection, the radiation levels along lateral, posterior and medial surfaces of the lower limbs were determined, using a Pitman isotope localization monitor, in conjunction with a 2.5 cm sodium iodide (thallium-activated) scintillation crystal.

A positive plot was indicated by the distribution along the symptomatic limb being markedly different from that along the asymptomatic limb. Of a total of 53 patients (with swollen calf and knee effusion), 36 gave positive, and 17 negative results. We were not aware of any false positives, but of the negatives, some patients probably had not sustained a synovial rupture, whilst undoubtedly some had a previous rupture which had subsequently become sealed off. Some patients showed an unusual distribution of isotope and this was thought to be due to the history of rheumatoid-arthritis, the bone and muscle structures accumulating the tracer medium to such an extent that localization of synovial fluid was not possible.

QUANTITATION OF ^{99}Tc^{m}-PHOSPHATE UPTAKE BY EMISSION TOMOGRAPHY

By P. H. Jarritt and P. J. Ell

The Middlesex Hospital Medical School, London W1

Emission tomography has the ability to provide accurate quantitation of radiopharmaceutical distribution within an image. The installation of the Cleon-710 transverse section imager at The Middlesex Hospital Medical School has allowed the assessment of its usefulness in quantitating ^{99}Tc^{m}-phosphate uptake within the skull.

Forty patients undergoing routine bone scanning using 15 mCi of ^{99}Tc^{m}-methyldiphosphonate (MDP) or ^{99}Tc^{m}-imidodiphosphonate (IDP) were subsequently imaged tomographically. One or two slices were obtained 4.5–6.0 cm above and parallel to the EAM with a scanning time of four or five minutes. The peak count rate obtained for each patient was corrected for scan time and radioactive decay and converted to values of μCi cm^{-3} using previously determined conversion factors. Normal ranges obtained for MDP and IDP were 0.16 ± 0.03 μCi cm^{-3} and 0.27 ± 0.09 μCi cm^{-3} respectively. From 20 abnormal patients with diffuse and focal disease, values were found from 2–10× above the normal range.

Data was presented showing the resolution of structures at the skull base; original images of the spinal canal and thoracic vertebrae indicate the scope of tomographic imaging in the future diagnosis of bone disease.

Book review

Atlas of Endoscopic Retrograde Cholangiopancreatography. Edited by E. T. Stewart, J. A. Vennes and J. E. Geenen, pp. xvi + 366 illus. 1977 (C. V. Mosby, St. Louis). £35·45.

Dr. Margulis in his Foreword states that the atlas is valuable because "it is the result of a true partnership between gastro-enterologist and radiologist. . .". No-one would question this. In fact there are 17 contributors of whom nine are physicians and eight are radiologists, and in essence the bulk of the book is a synthesis of the clinical experiences of these authors. There are over 200 case illustrations of normal and abnormal findings and they are presented with some brief clinical information, X-rays (often of mediocre reproduction but meticulously labelled), a thorough description of the X-ray and rounded off with some useful comments where appropriate. The first four chapters deal with technical aspects, including radiology, which although helpful are clearly no substitute for apprenticeship. Chapter 5 is a reminder of the embryological development of the pancreatic and biliary systems which is essential for understanding the developmental anomalies of adult life. The final chapter is a very brief account of endoscopic papillotomy for removal of common duct stones, which is adequate for most endoscopists in this country as they will not be attempting this procedure.

ERCP has undoubtedly been a major advance in the investigation of jaundiced patients and those with pancreatic disease. The investigation of first choice, however, is now abdominal ultrasound which is entirely non-invasive, and when dilated bile ducts are found Chiba needle cholangiography should be the next step. This is safe, cheap and requires minimal expertise. Not so with ERCP as the duodenoscope may cost in excess of £5000, considerable experience is required and as stated in chapter 4 has the highest complication rate of all current diagnostic gastro-enterological techniques (2.3%). Notwithstanding this, no technique reveals the pancreatic ducts with such clarity and the atlas illustrates many fine examples of the duct changes in, for instance carcinoma of the pancreas and chronic pancreatitis. There are also examples of sclerosing cholangitis and high biliary strictures which often may only be adequately evaluated with retrograde cannulation. Thus, in spite of the contracting indications for ERCP and the rather lower position it now occupies in the diagnostic flow-chart, this comprehensive volume is a worthwhile and welcome addition. The atlas is rather expensive, but it is hoped that it will find its way into the reference libraries available to all those who practise and study gastro-intestinal endoscopy and radiology.

R. ZEEGEN.

Forthcoming events and other notices

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

RADIOBIOLOGY MEETING

"Preview of papers for the International Congress, Japan". April 20, 1979. This will be a general meeting, and proffered papers are invited. Titles and brief preliminary abstracts should reach Dr. J. H. Hendry, Paterson Laboratories, Christie Hospital and Holt Radium Institute, Manchester M20 9BX by March 15, 1979.

Further information can be obtained from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London WIM 7PG (01-935 6237).

SPRING MEETING IN NEWCASTLE

A joint meeting organized by the Royal College of Radiologists and The British Institute of Radiology to be held March 30–31, 1979.

All enquiries, including requests for programme and registration forms should be made to the Royal College of Radiologists, 38 Portland Place, London W1.

AN ADVANCED COURSE IN CARDIAC ULTRASOUND

This course, to be held at Harefield Hospital, April 23–27, 1979, is intended for doctors and technicians already working in the field or with some knowledge of the subject. It will be under the direction of Ronald Pridie and Stuart Hunter. Other speakers will include Derek Gibson, Grahame Leach, Robert Anderson, John Gore and Dan Thunstall-Pedoe.

Residential accommodation is available. Applications to: Mrs. L. Grieve, Ultrasound Department, Harefield Hospital, Harefield, Middlesex.

1979 THE BRITISH INSTITUTE OF RADIOLOGY ANNUAL CONGRESS

The 37th British Institute of Radiology Annual Congress and Scientific Exhibition will be held at the Middlesex Hospital Medical School on April 26–27, 1979. Included in a programme of invited papers on diagnosis, therapy, radiological physics and nuclear medicine topics will be the Presidential Address by Mr. W. M. Ross entitled *The Institute, yesterday and tomorrow*, and the Silvanus Thompson Memorial Lecture by Professor G. E. Adams on *Past, present and future of hypoxic cell sensitizers*.

Details and registration from The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

FUNDAMENTALS IN TECHNICAL PROGRESS IN ULTRASOUND, DOSE PLANNING AND DATA PROCESSING IN NUCLEAR MEDICINE

An International Symposium to be held at the University of Liège (Sart-Tilman) on May 11–12, 1979. It will include invited papers by universities specialists and manufacture engineers, tending to present an approach of a concerted plan for developments in the near future.

Further information from Dr. J. Garsou, Agrégé, Contrôle Physique Radiations, Radiothérapie, 59 Boulevard de la Constitution, B-4020 Liège.

EUROPEAN CONGRESS OF XERORADIOLOGY

A congress of xeroradiology organized by the Fondazione Internazionale Menarini will be held in Venice, Italy from May 11–13, 1979 inclusive.

The three day programme will include invited and proffered papers and teaching seminars on all aspects of xeroradiographic techniques, imaging and directions of future development.

Further information may be obtained from the Organizing Committee, European Congress of Xeroradiology, Dott. ssa Angela Peroni, Fondazione Menarini Internazionale, Piazza Del Carmine 4, 20100 Milan, Italy.

THIRD EUROPEAN NUCLEAR MEDICINE SOCIETY MEETING

This meeting will be held in Karlovy Vary, Czechoslovakia, May 15–18, 1979 and is organized by the Czechoslovak Society of Nuclear Medicine and Radiation Hygiene.

The official languages will be English, French, German and Russian and simultaneous interpretation will be provided.

Registration: Czechoslovak Medical Society, J. E. Purkyne, 3rd European Congress of Nuclear Medicine, Sokolská 21, 120 26 Praha 2, Czechoslovakia.

CONVERSAZIONE

The British Institute of Radiology Conversazione will be held at the new Royal College of Radiologists house at 38 Portland Place, London on May 16, 1979.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

MACKENZIE DAVIDSON MEMORIAL LECTURE

To be given by Dr. G. B. Schofield, Medical Officer, British Nuclear Fuels Ltd., on *Biological control in a plutonium production facility* at The British Institute of Radiology, 32 Welbeck Street, London, W1 on Thursday, May 17, 1979.

PAEDIATRIC RADIOLOGY

A two-day course in diagnostic paediatric imaging will be held at the Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London, WC1 on May 17–18, 1979. The main theme of this course will be the thorax. Further details and application forms are available from The Secretary, Department of Paediatric Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JN.

INTERNATIONAL SYMPOSIUM ON INTERVENTIONAL RADIOLOGY

An E.A.R. Symposium, organized by the Portuguese Society of Radiology and Nuclear Medicine, will be held May 30–June 2, 1979 in the Algarve, Portugal.

Proposed sessions include vascular therapy; selective embolization and management; catheter implantation in chemotherapy and percutaneous treatments; ultrasonic guiding techniques and nuclear imaging as a guiding technique for biopsy and fluid aspiration.

For further information contact the Portuguese Society of Radiology and Nuclear Medicine, 123, 1.° Esq., Avenida Elias Garcia, Lisbon 1, Portugal.

AN INTENSIVE COURSE IN CHEST AND RENAL RADIOLOGICAL DISEASES

The course, to be conducted in Johannesburg from May 31–June 3, 1979, will cover all general principles as well as the most modern techniques and recent advances such as ultrasonography, CT scans etc.

The renal section will be conducted by Prof. Harry Mellins of the Peter Bent Brigham Hospital, Boston, USA. The chest section will be covered by Prof. Manuel Viamonte of the Mount Sinai Hospital, Miami, Florida, USA. Registration fee will be R80.00.

It may be possible to arrange special reduced group air fares from the USA, UK and Europe depending on the number of delegates attending from the respective countries. Further enquiries can be made to the Director and Organizer; Dr. Pete Reichman, PO Box 2251, Johannesburg 2000, South Africa, tel. (110) 37-6060.

Non-Invasive Imaging in Medicine: Heart, Liver, Pancreas

A Symposium arranged by the medical faculty of the University of Lund, Sweden, on June 6–9, 1979, with participation of prominent speakers in the field of CT-scanning, ultrasonography, and nuclear scanning.

For further details and registration, contact Miss Karin Jönsson (secr.), Department of Diagnostic Radiology, University Hospital, S-221 85 Lund, Sweden.

International Course in Chest Radiology

International Course in Chest Radiology and other aspects of chest disease, Stockholm, Sweden, June 11–13, 1979.

Organized by the *Fleischner Society*, a non-profit organization in memory of Felix Fleischner, Harvard University, Boston.

Information and application forms from: Björn Nordenström, M.D., Professor of Radiology, c/o Reso Congress Service, S-105 24 Stockholm, Sweden.

Nuclear Cardiology

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on June 20, 1979 at St. Bartholomew's Hospital, Gloucester House, Little Britain, London, EC1. Anyone wishing to make a presentation should contact Dr. K. E. Britton, St. Bartholomew's Hospital.

Further information regarding this meeting can be obtained from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

IV European Congress of Radiology

The IV European Congress of Radiology will take place in Hamburg (German Federal Republic), September 4–8, 1979.

Scientific programme:

diagnostic research of organs of the upper abdomen;

diagnostic research in nuclear medicine: organs of the upper abdomen;

radiotherapy in tumours of the genital system of males and females;

radiobiology and X-ray protection (combined therapies and risks of ray exposure);

radiophysics and techniques (methodical problems in diagnostics and in planning of radiotherapy).

Enquiries: Secretary of the IV European Congress of Radiology, Postfach 10 64 07, D-2000 Hamburg 1, Federal German Republic.

Quantitation of Tumour Response: a Critical Appraisal

The L. H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to simulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.

Factors of prognostic significance.

In vitro assays of tumours excised after treatment *in vivo*.

The choice of suitable experimental models in rodents.

The role of human tumour xenografts.

Statistical evaluation of tumour response data.

The limitations and artefacts of each assay technique.

The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

British Association of Clinical Anatomists

Owing to unforeseen circumstances it has been necessary to change the date of the Summer Meeting at the University of Manchester; it will now be held on Wednesday September 26, 1979 (not May 11 as previously announced).

Further details about the Associates may be obtained from the Secretary, Professor R. K. H. McMinn, Royal College of Surgeons, 35–43 Lincoln's Inn Fields, London WC2A 3PN.

VII International Congress of Lymphology

Professors E. Tosatti and E. Cariati are respectively honorary president and president of the above meeting to be held in Florence October 28–November 2, 1979. The official language will be English with simultaneous translation in French, German and Italian. There will be sessions dedicated to methodology, physiology, pathology, drug interaction, treatment of tumours, classification of non-Hodgkin's lymphomas, pulmonary hypertension etc. Two postgraduate courses on lymphodemas and Hodgkin's disease are also planned.

Scientific information: Professor E. Cariati, Clinica Chirurgica "R", V. le Benedetto XV, Genoa, Italy.

Organizing secretariat: O.I.C. Via Dei Bardi 52, 50125 Florence, Italy.

Symposium on Spine and its Contents

E.A.R. "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in the:

(a) Equipments and investigative methods of spine and spinal cord.
(b) Radioanatomy and physiology of spine and spinal cord.
(c) Radiodiagnosis of pathological conditions.
(d) Interventive (diapeutic) radiodiagnostic methods.

For further information contact (not later than June 1979): The secretariate of "Vertebro 1980", P.O.B. 88, Sokolská 31, 120 26 Praha 2, Czechoslovakia.

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Book received

Receipt of the following book is acknowledged as a courtesy to the sender. This will not be reviewed in detail in THE BRITISH JOURNAL OF RADIOLOGY.

International Directory of specialized cancer research and treatment establishments. 2nd Edition. Published under the auspices of the Committee on International Collaborative activities (CICA), 1978, pp. xviii+724 UICC Technical Report Series vol. 33 (International Union Against Cancer, Switzerland) Sw.fr.100.

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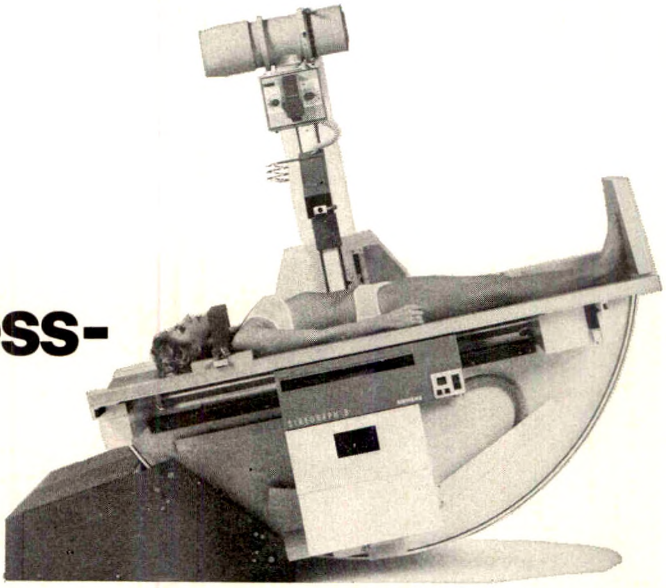

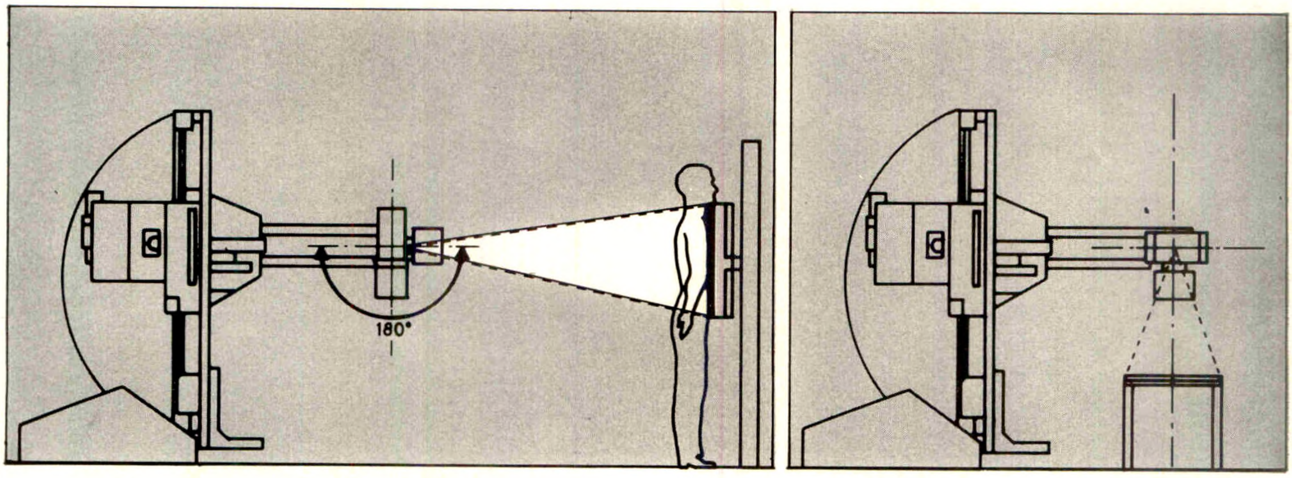

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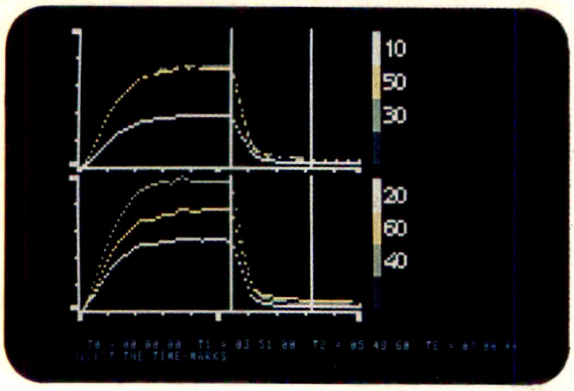

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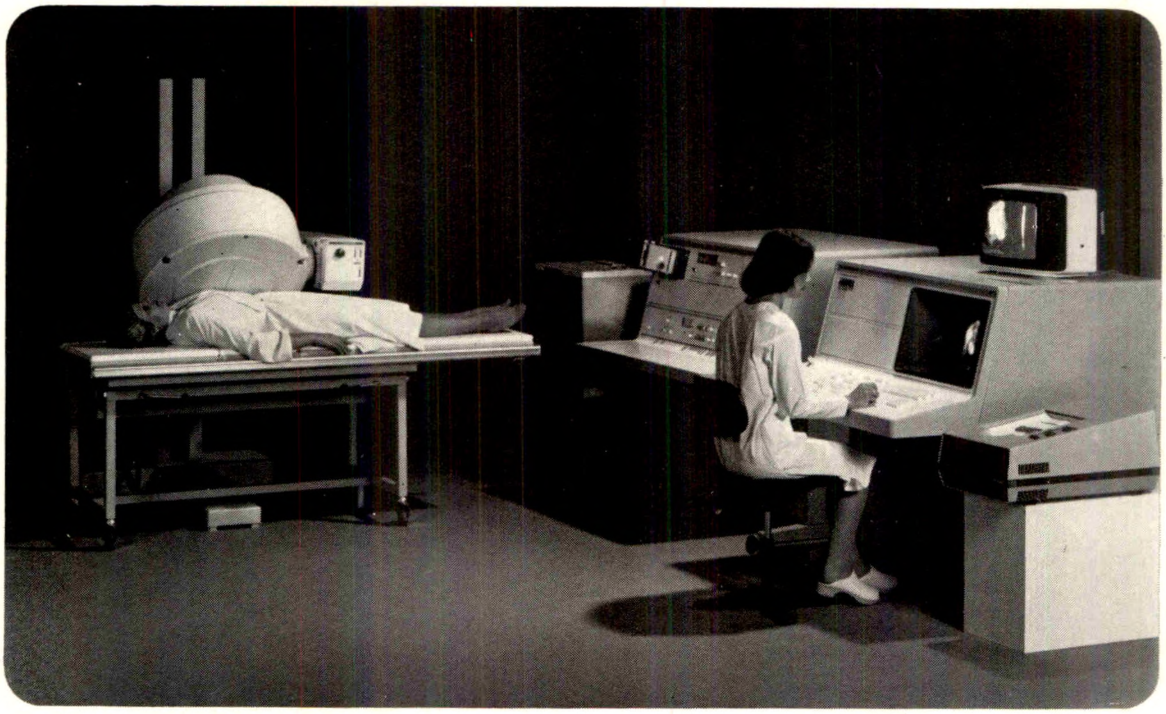

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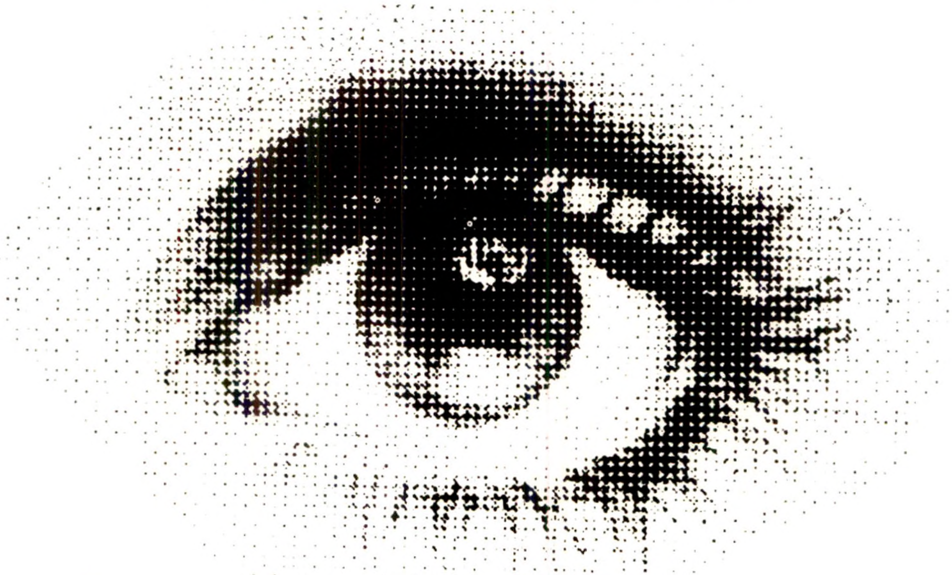

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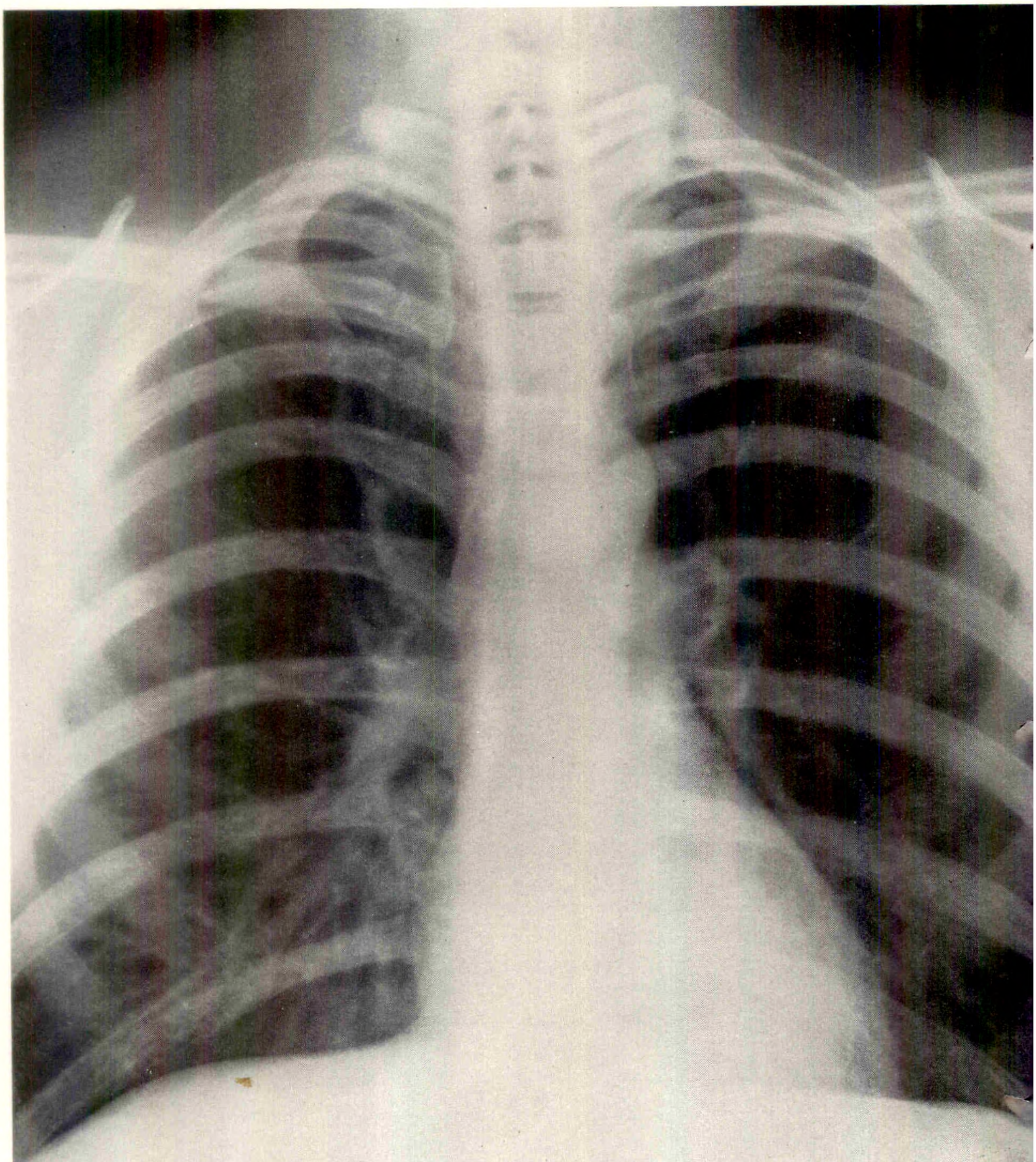

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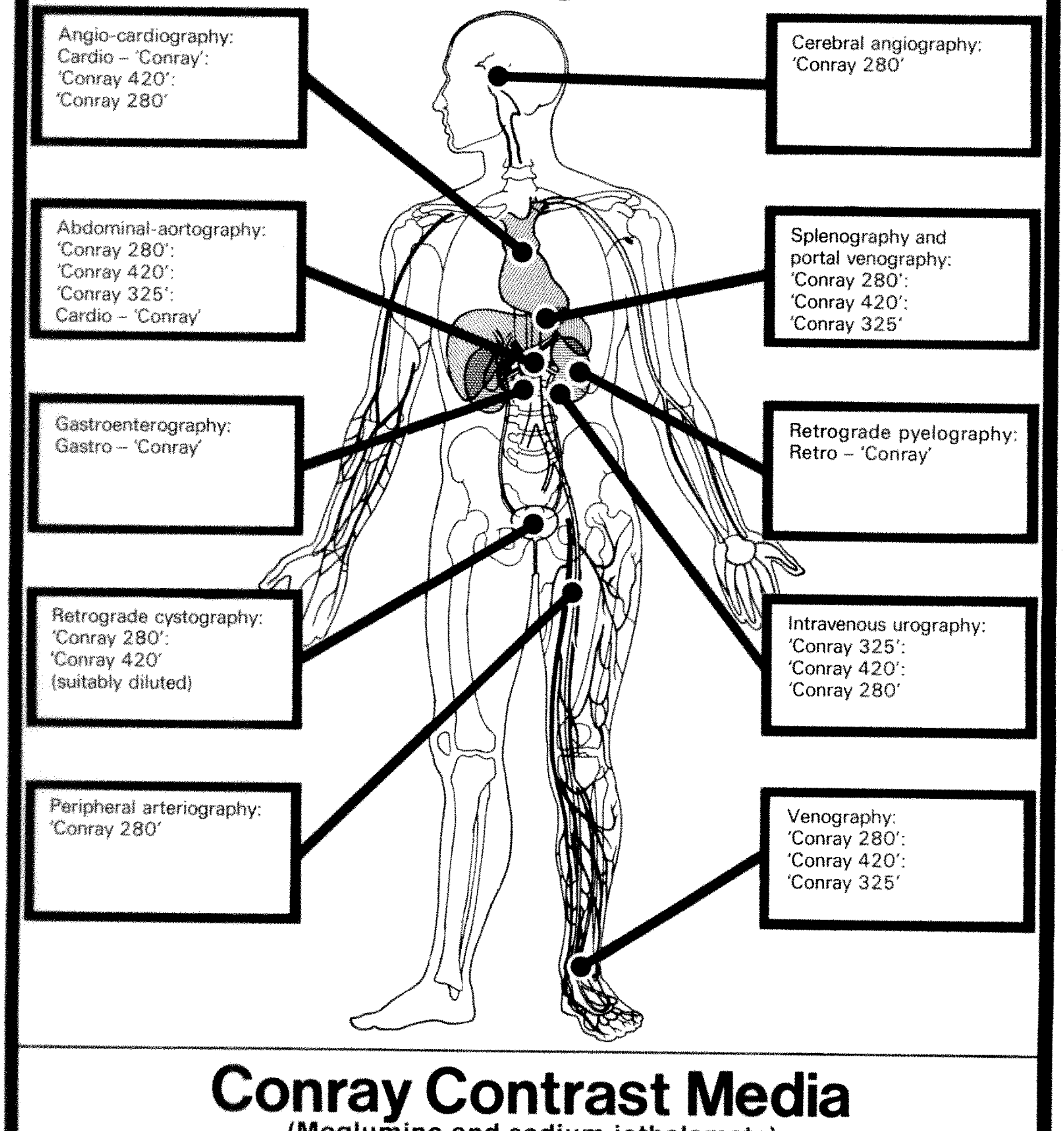

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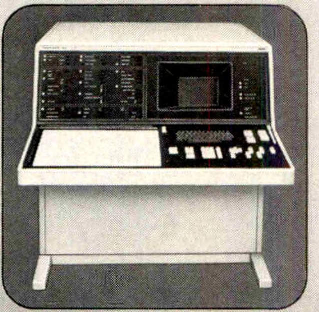

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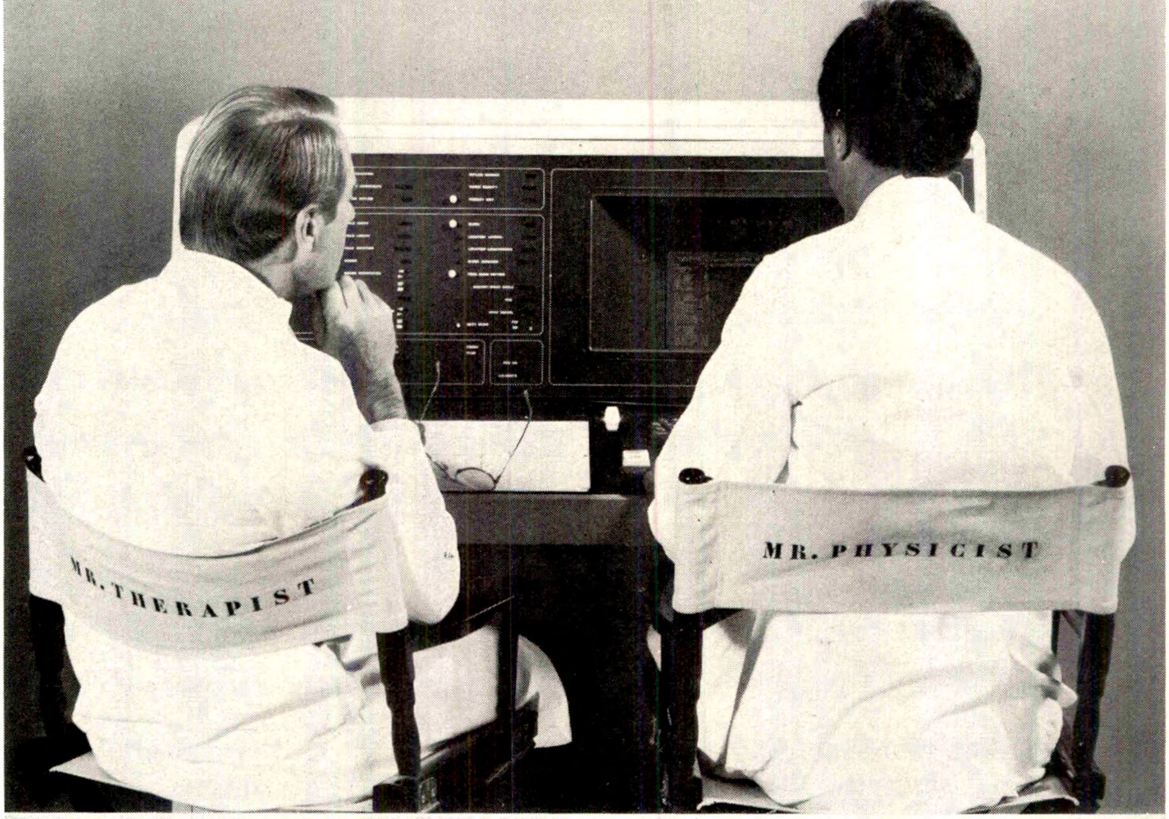

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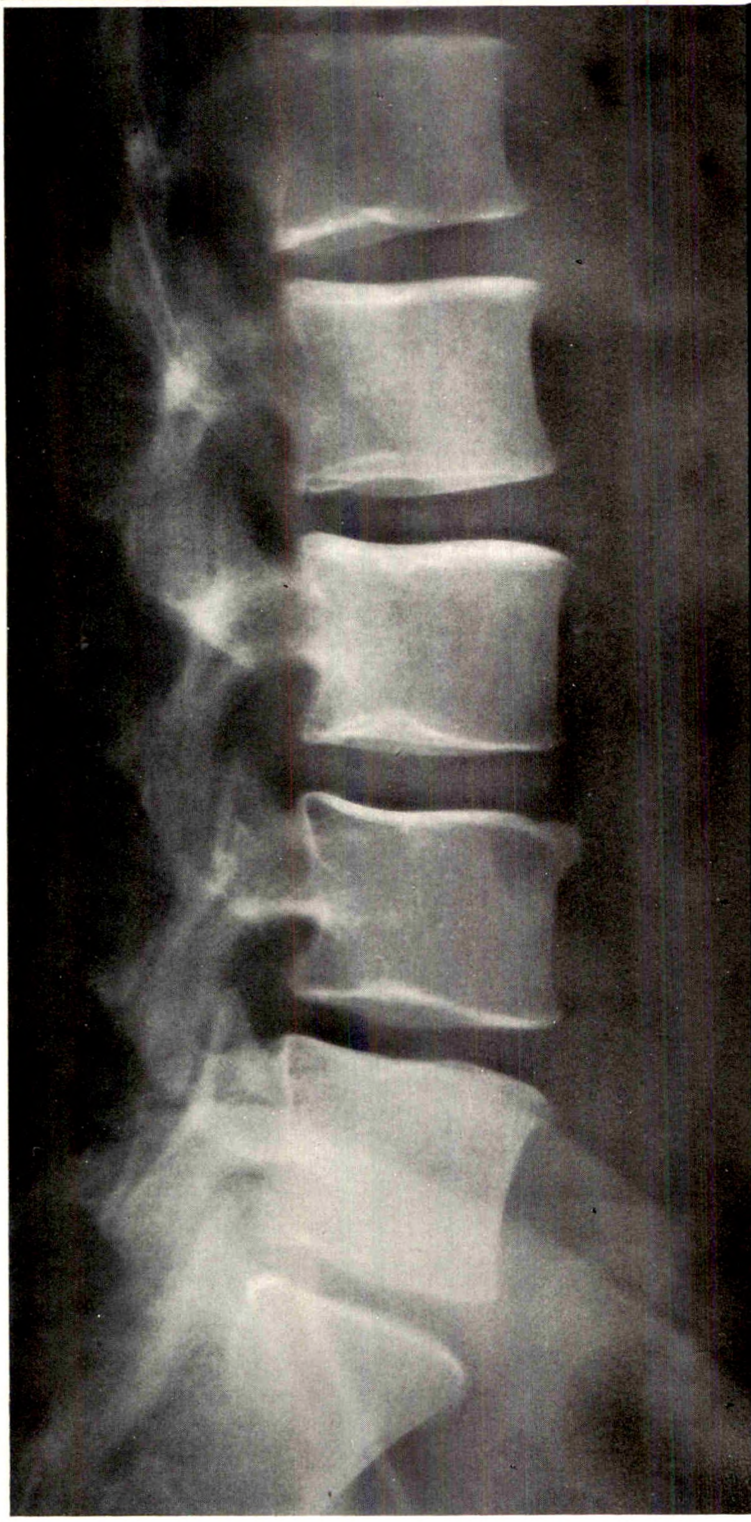

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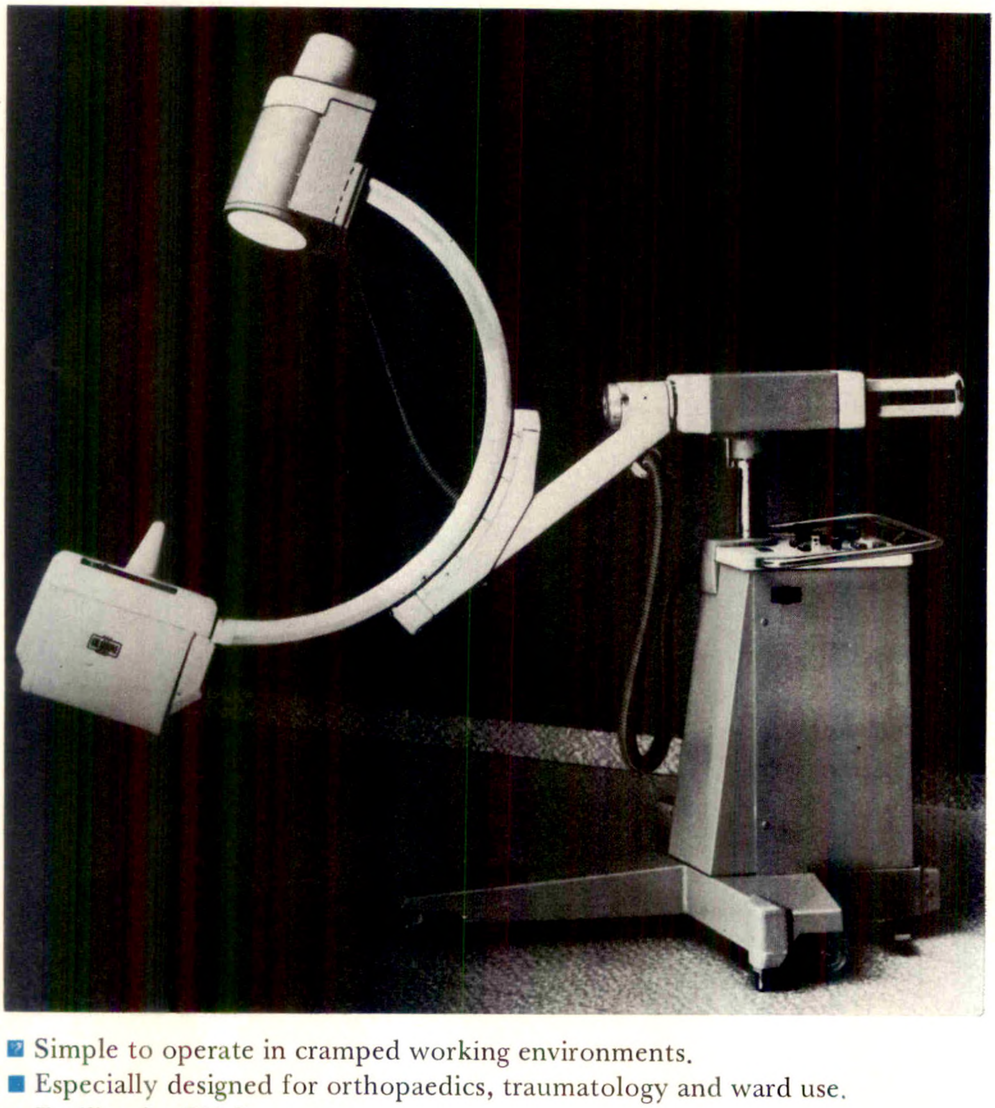

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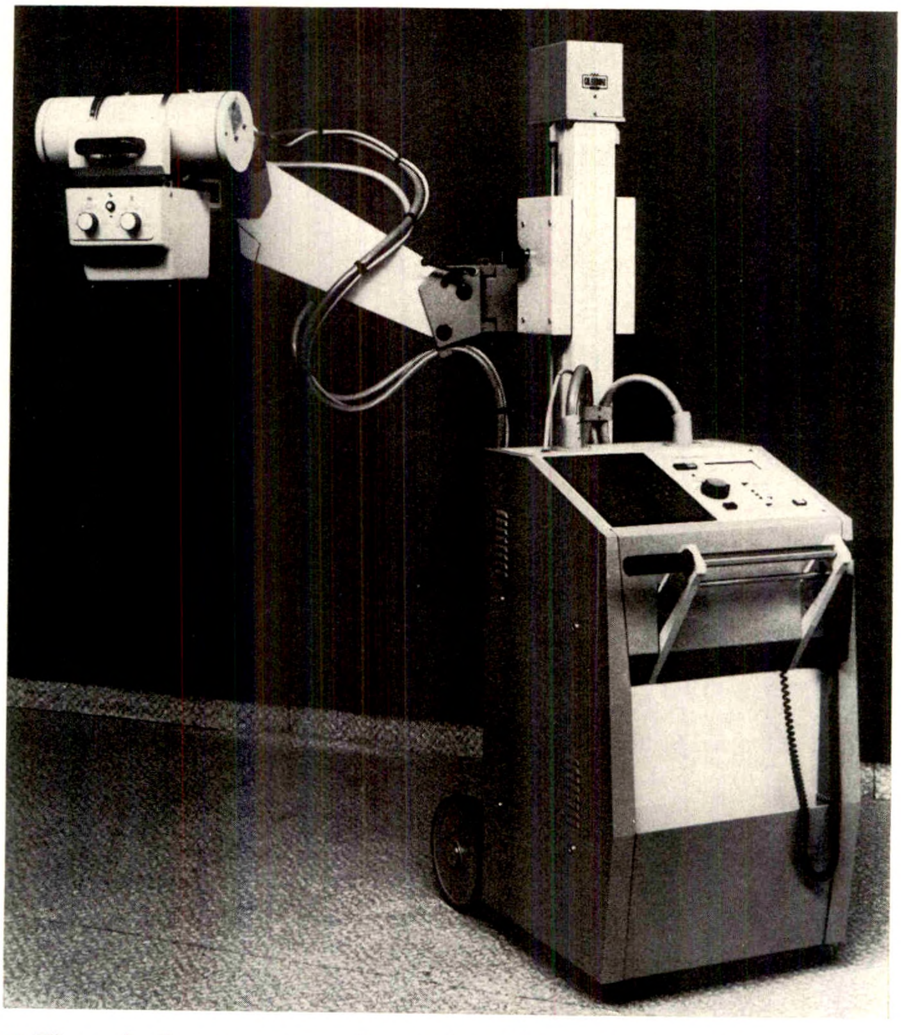

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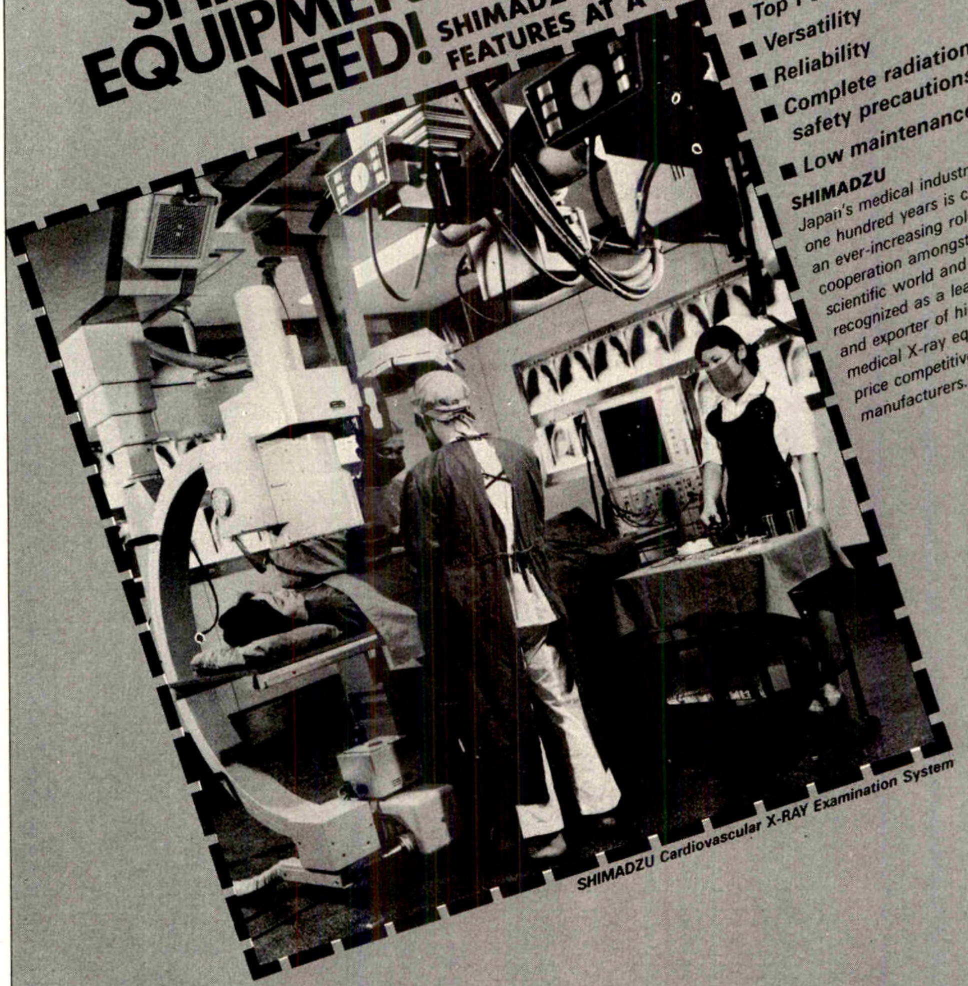

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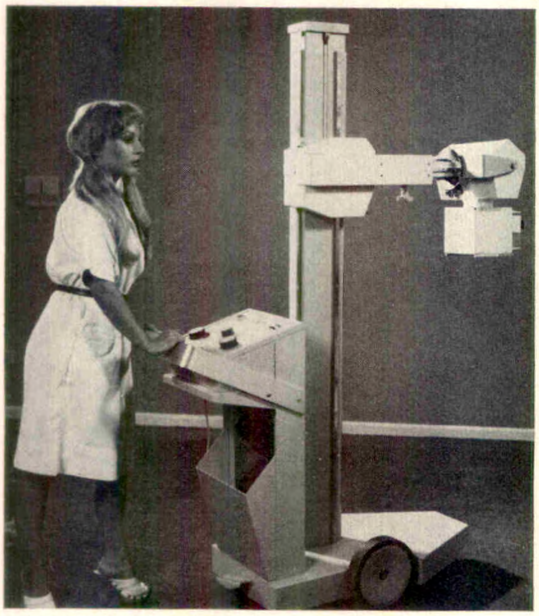

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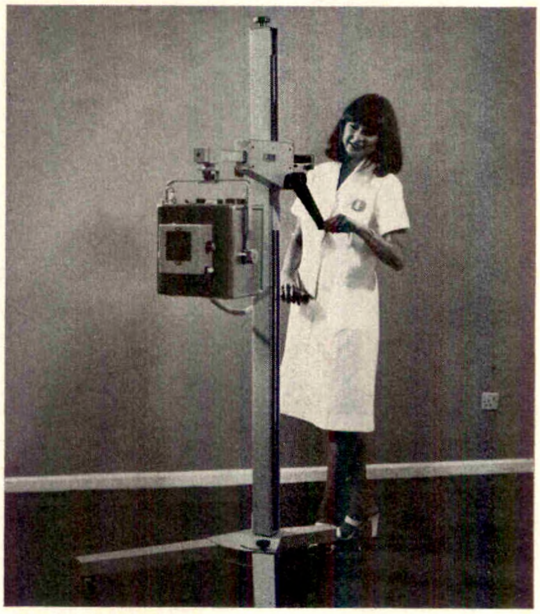

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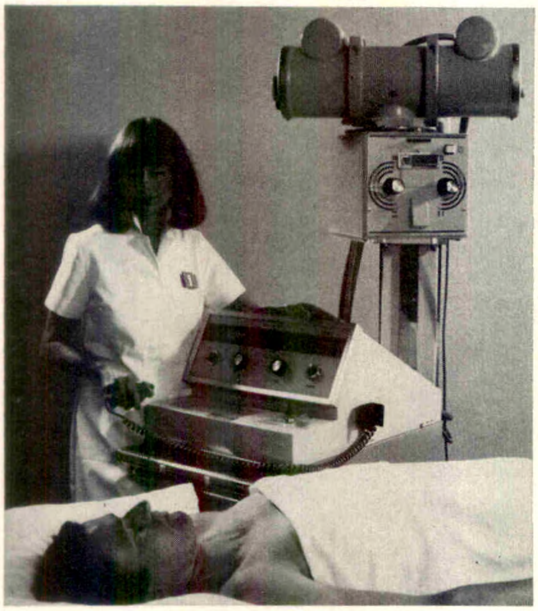

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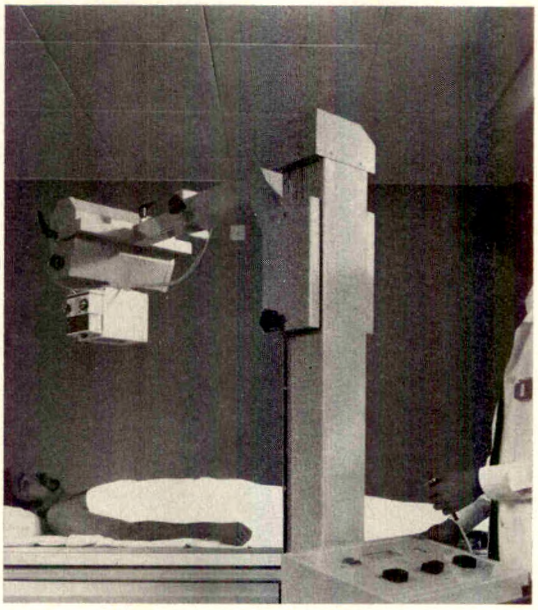

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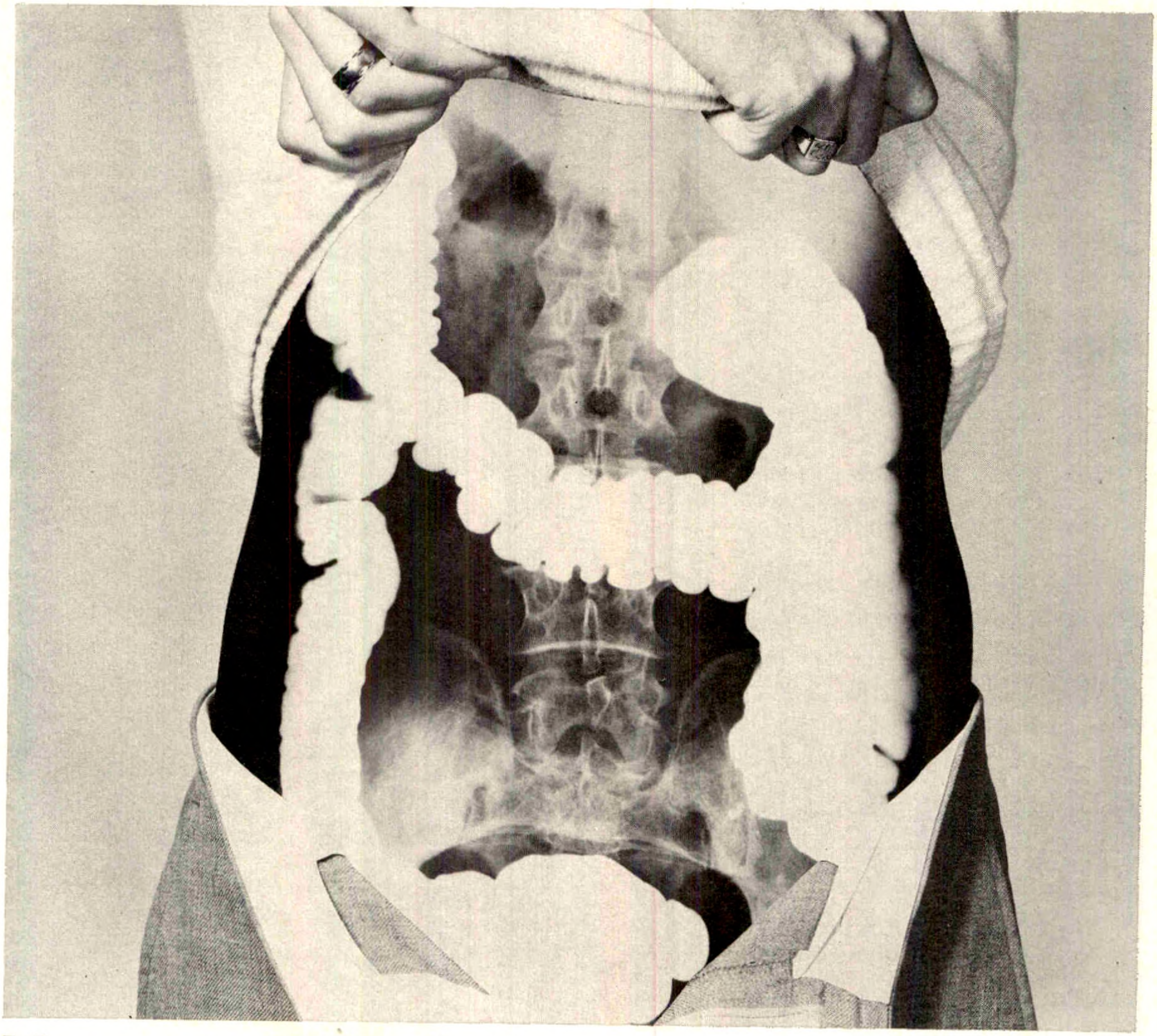

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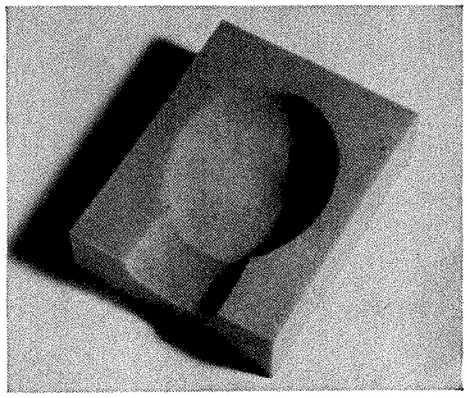

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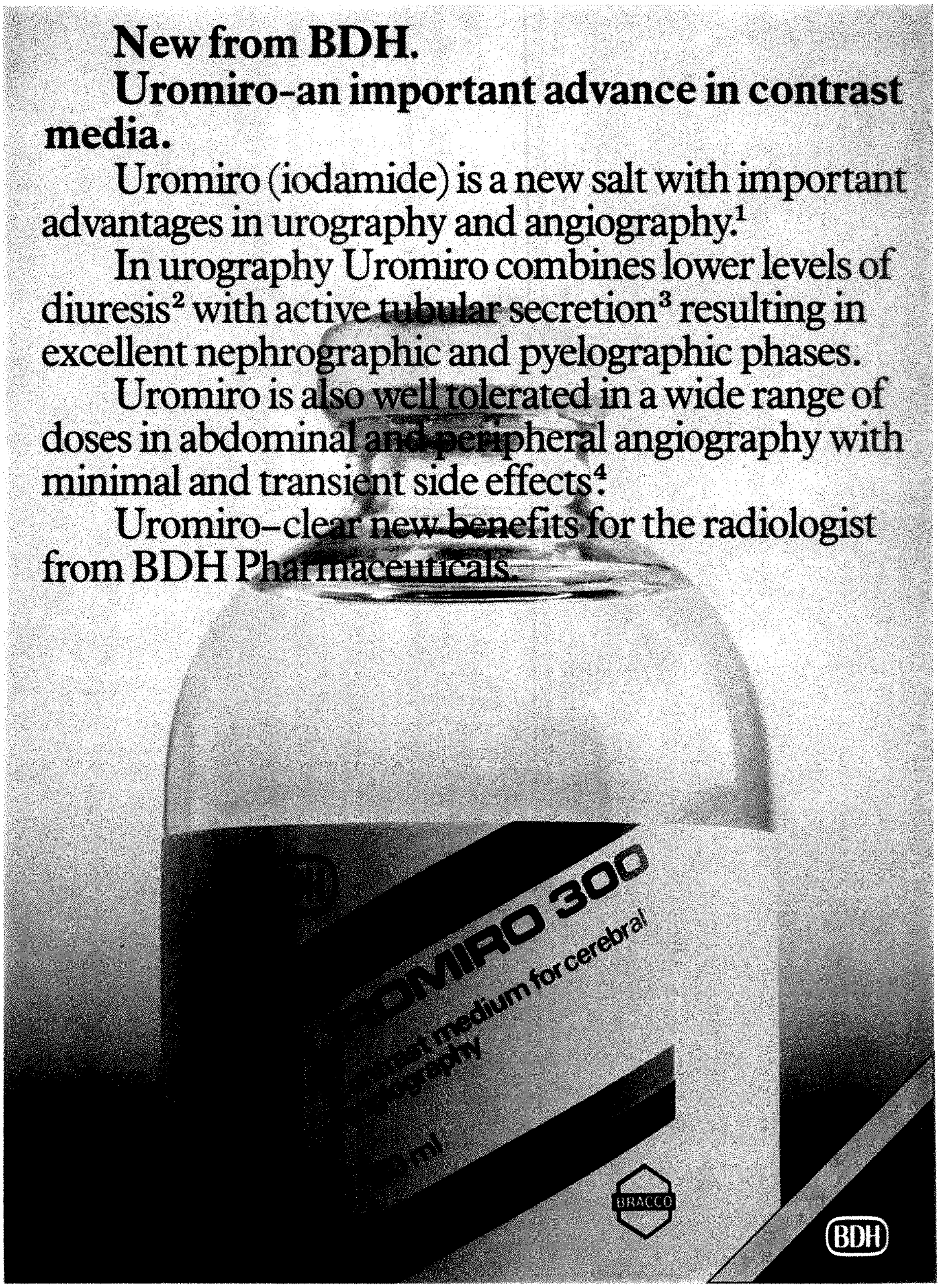

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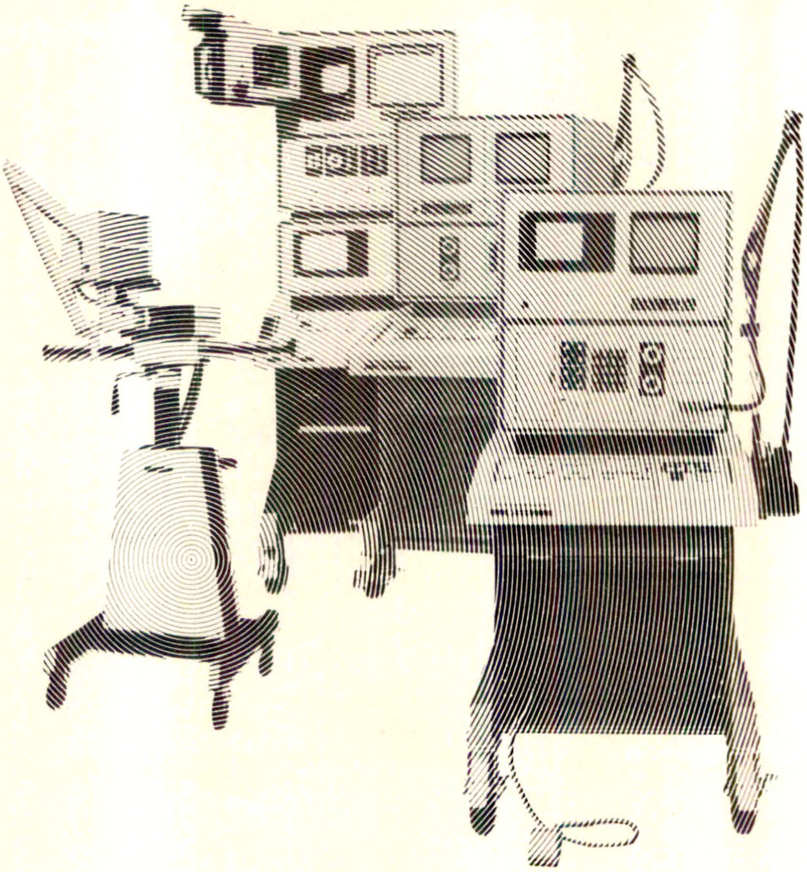

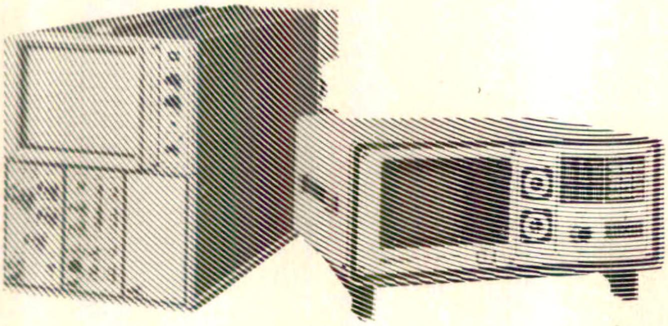

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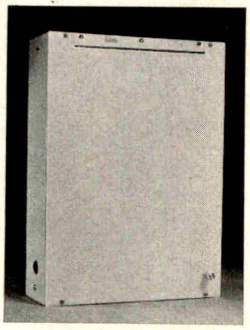

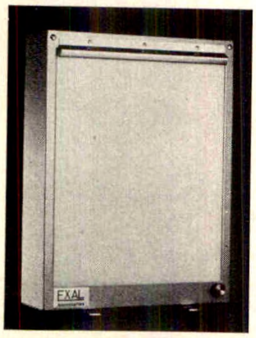

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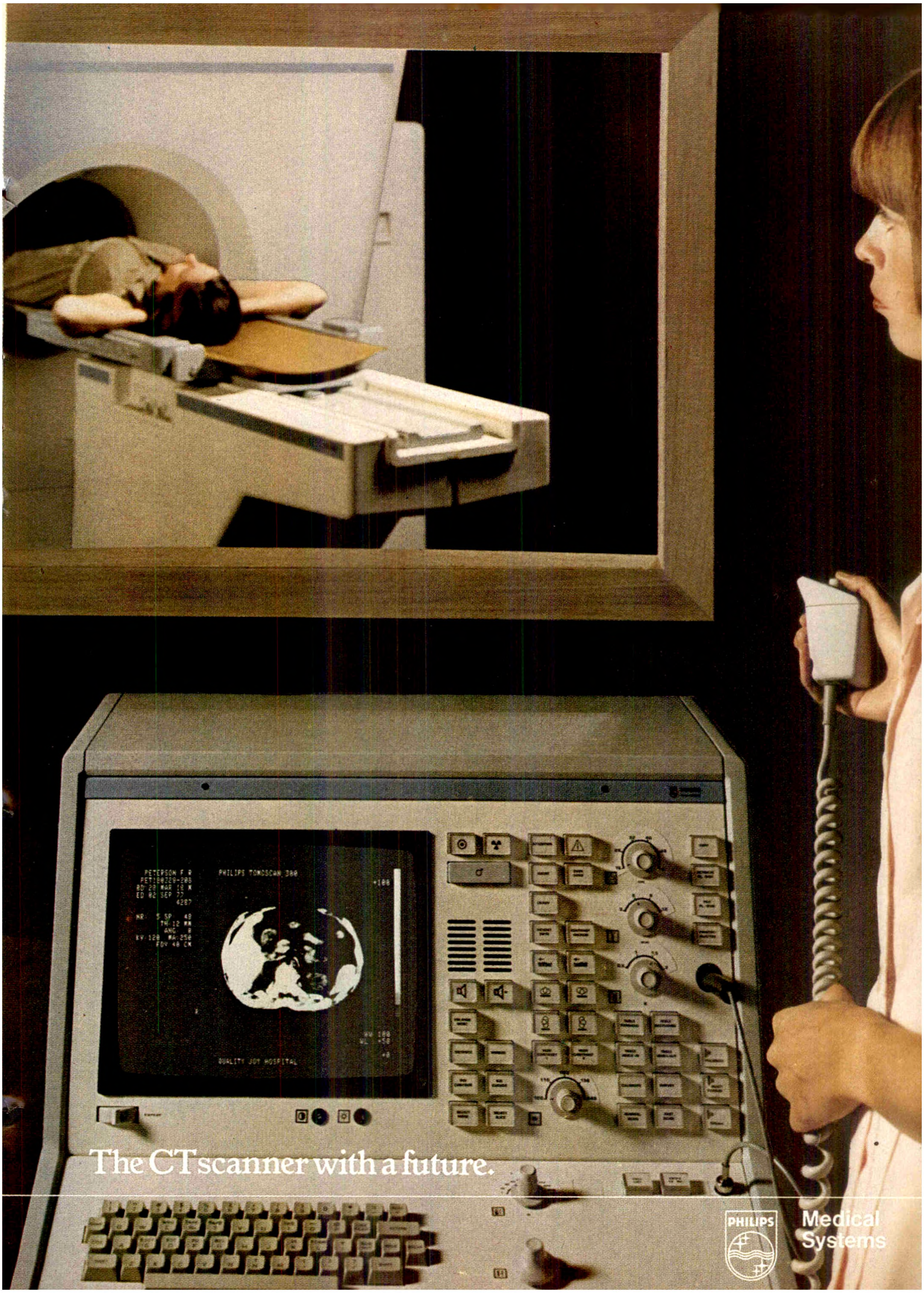
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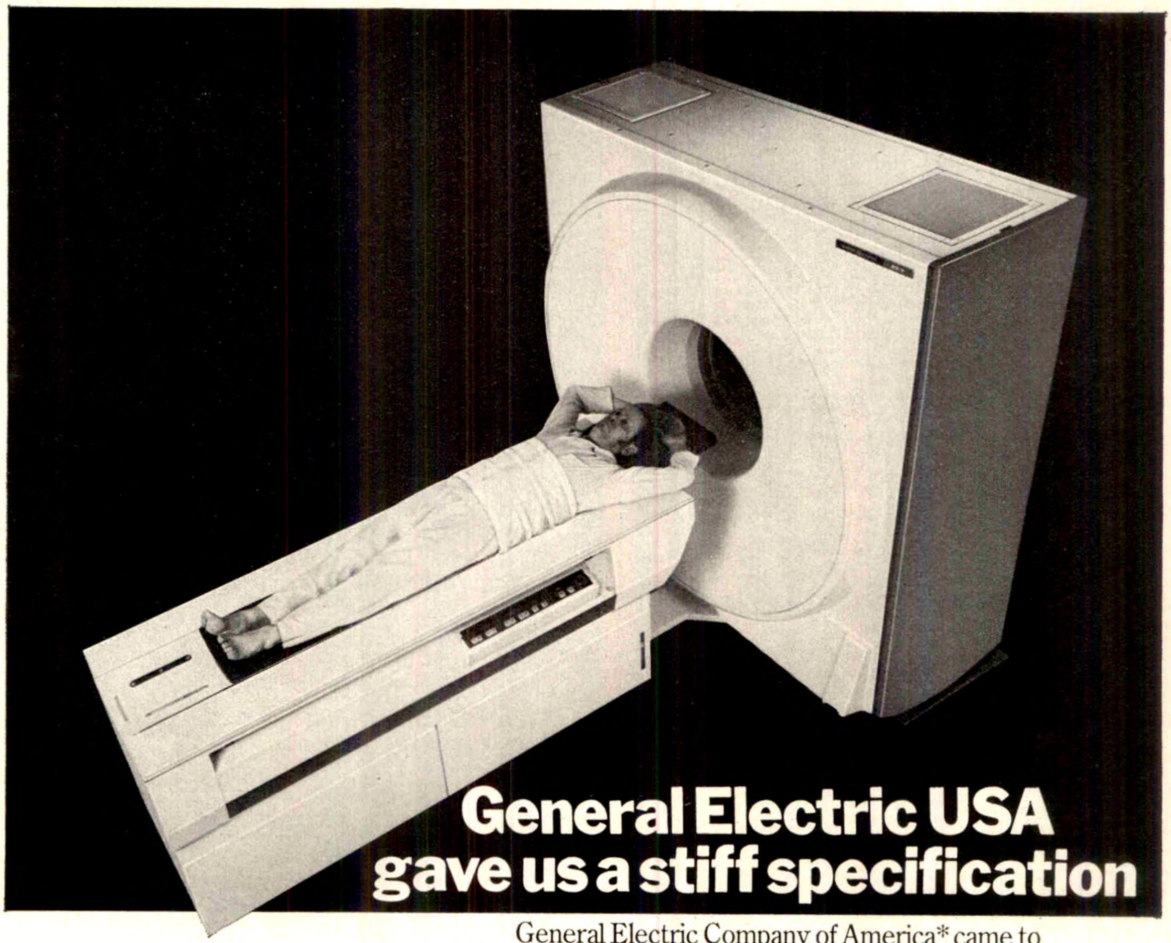

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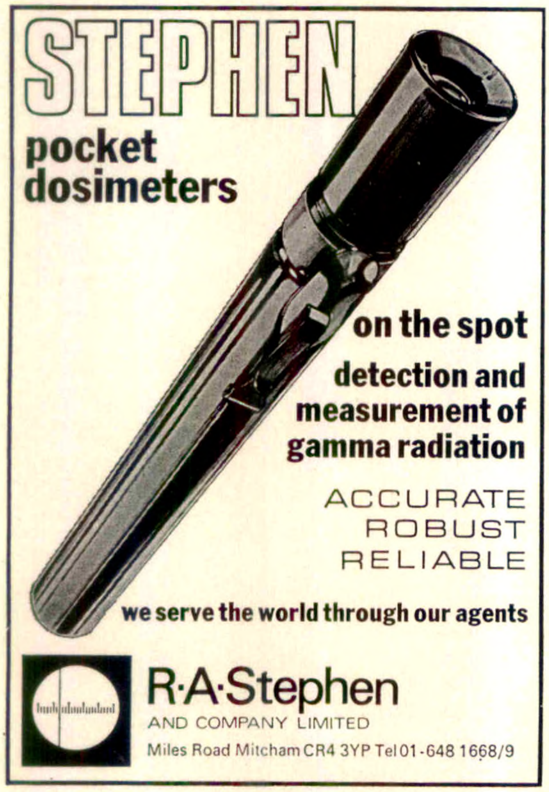

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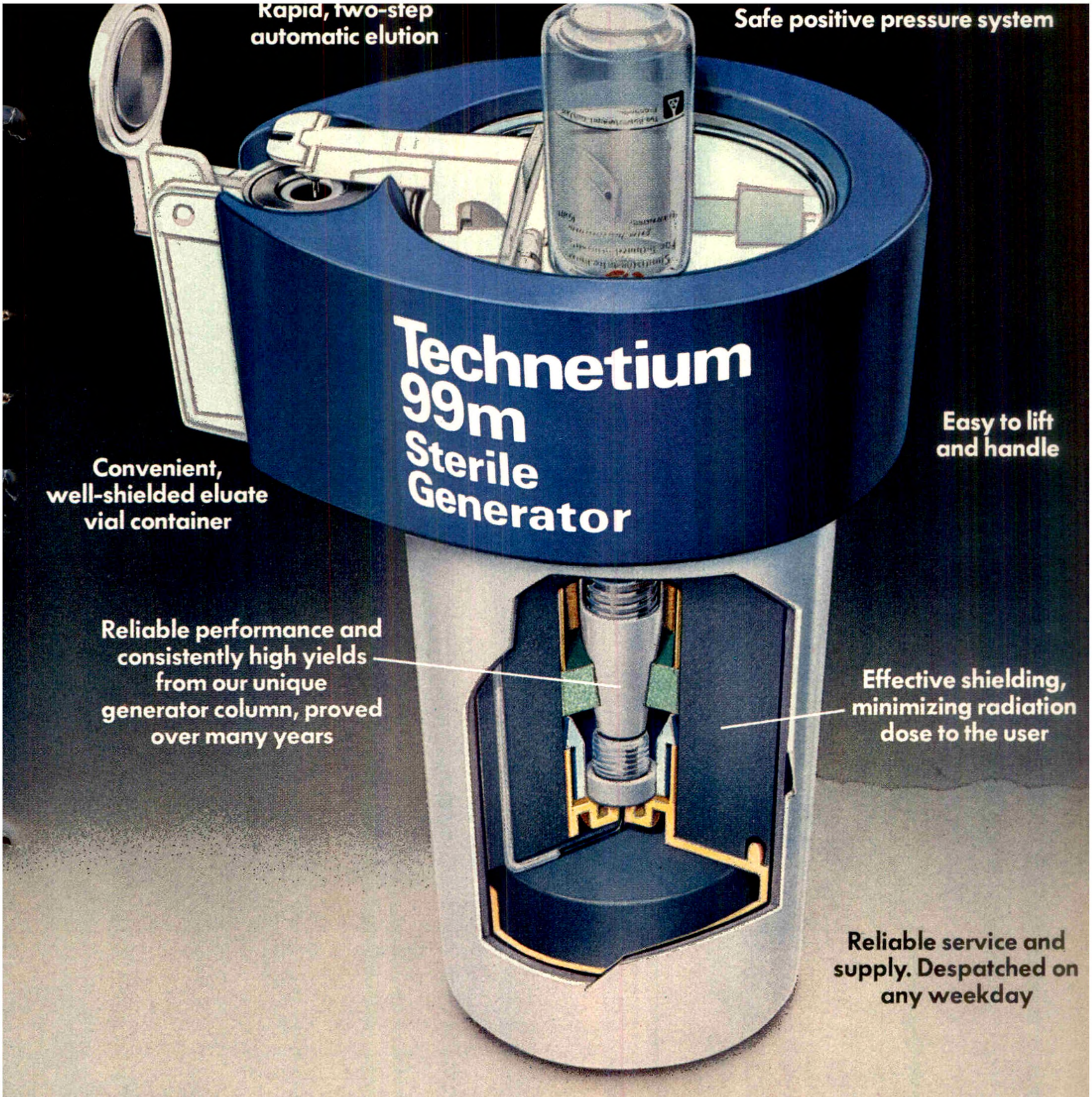
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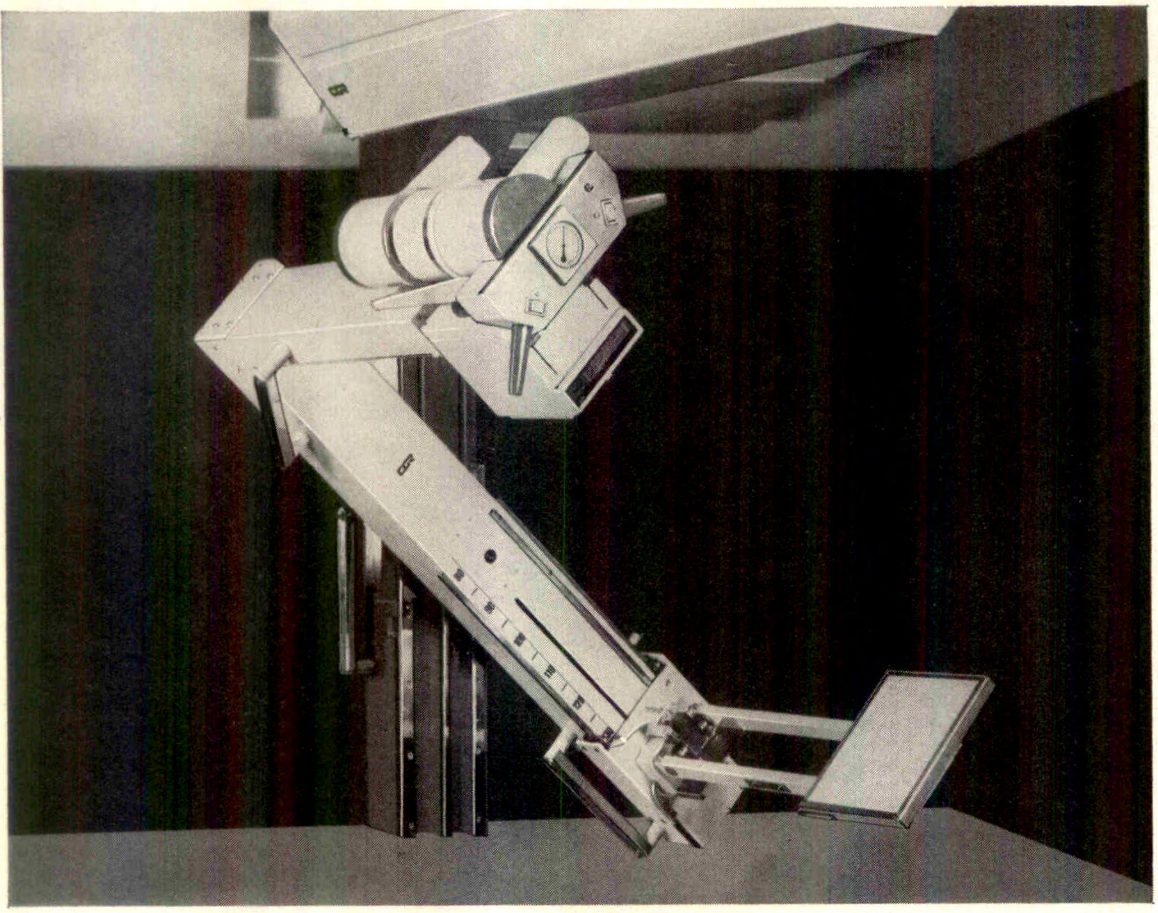

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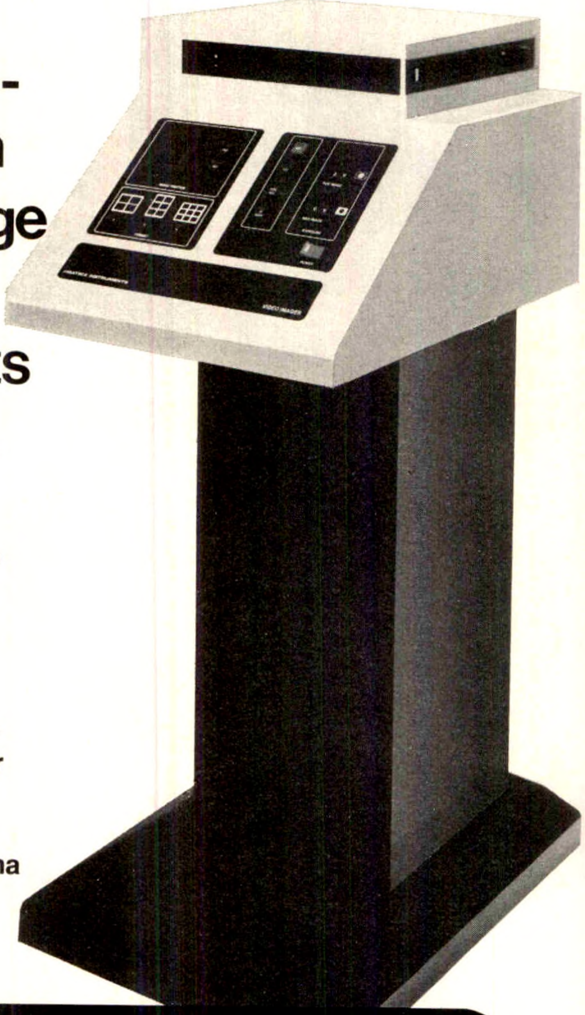

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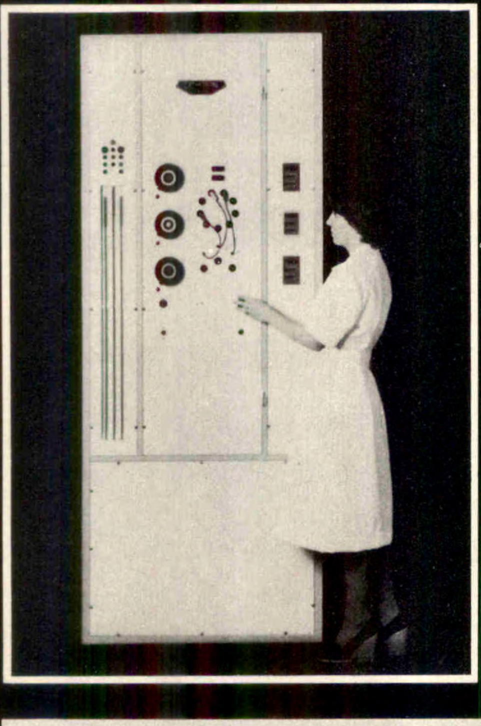

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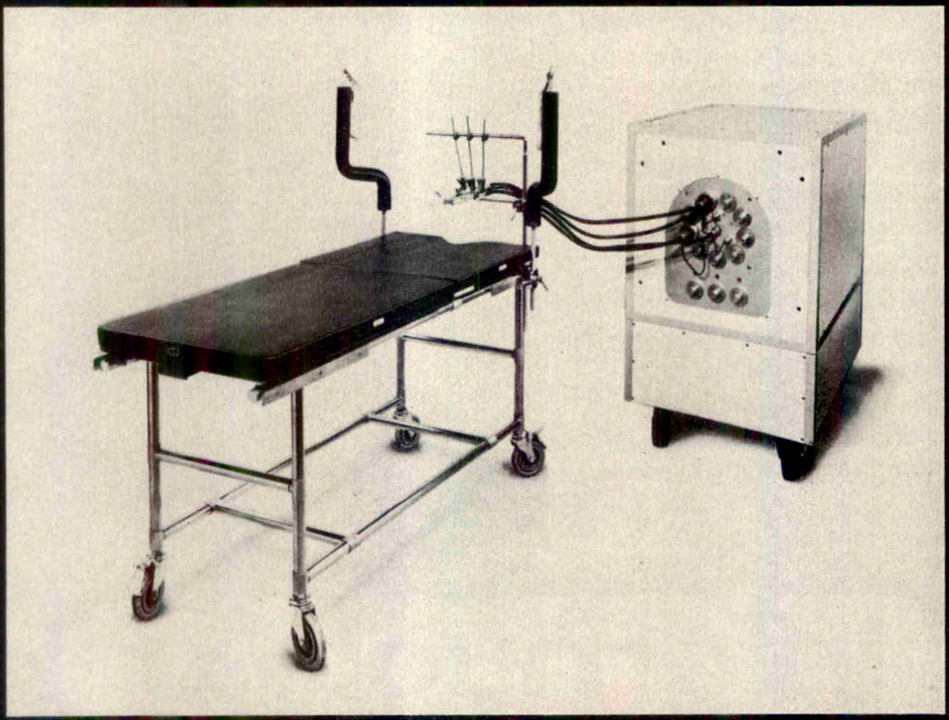

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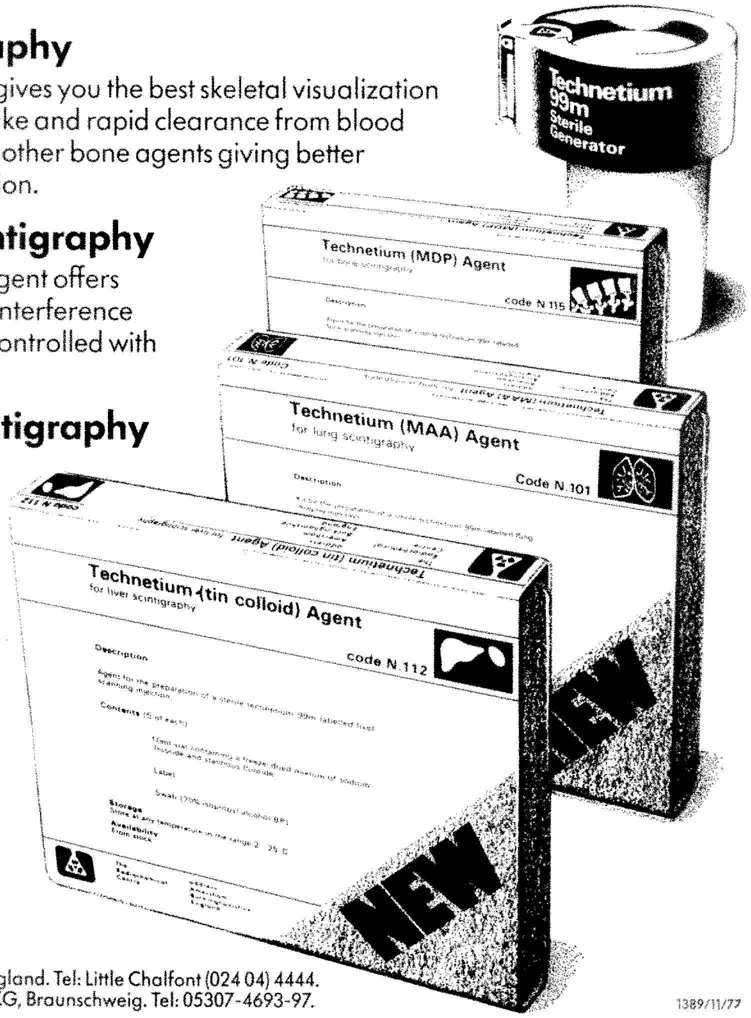

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A radiological approach to infertility—hysterosalpingography

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ABSTRACT.

The hysterosalpingograms of 98 patients with infertility were reviewed with reference to technical problems, radiological features of each pathology and accuracy of reporting. Findings were confirmed by review of the reports of laparotomy or laparoscopy on all patients.

Of the total number of fallopian tubes investigated (196), 70 hydrosalpinges were correctly diagnosed from a total of 77. Agreement between HSG and operation was achieved in 123 of 127 fallopian tubes with peritubal adhesions, in all six of those with cornual spasm and in eight with cornual occlusion. In 16 of 20 fallopian tubes with partial distal occlusion, reporting was correct.

With the potential accuracy of HSG diagnosis, we contend that it should be a preliminary procedure in every case, and in many may be the only investigation of tubal patency required prior to surgery or conservative management.

Hysterosalpingography (HSG) has for many years been an invaluable procedure for the assessment of tubal patency and tubal and intra-uterine pathology (Siegler, 1967b).

Recently the use of laparoscopy for direct tubal visualization in the investigation of infertility has tended to replace HSG in many centres (Coltart, 1970; Frangenheim, 1967; Gabos, 1976; Maathuis *et al.*, 1972).

In the infertility clinic at Groote Schuur Hospital, where a large number of low socio-economic patients are investigated, 75% of 150 new patients seen annually have tubal obstruction as a contributory factor and more than 650 HSG's are performed (Annual Report, Obstetrics and Gynaecology Department, Groote Schuur Hospital, 1976). Because of the low risk (Siegler, 1967a) and potential accuracy of the procedure, the diagnosis prior to reparative surgery in many of these cases is made on HSG alone. Laparoscopy is reserved for those cases with cornual obstruction, inadequate HSG or such severe disease clinically and salpingographically that to perform surgery would be fruitless.

We have reviewed the place of HSG in our department with specific reference to technical problems, radiological features and accuracy of reporting with direct relevance to infertility.

As a result of our findings it is our contention that the HSG has a definite part to play as a preliminary procedure in every case, and because of the accuracy of the procedure in our hands, in many it is the only investigation of tubal patency required before surgery. This reduces the need for many laparoscopies, and hence the potential risks and expense of this procedure in a busy unit.

MATERIALS AND METHODS

Ninety-eight patients with infertility, investigated in our infertility clinic during the period January 1975 to March 1977 were reviewed with comparison of the radiological appearances at HSG and the appearances at laparotomy or laparoscopy. Preoperative HSG's were reviewed and reported. The findings were then compared with the operative notes of laparotomy or laparoscopy.

Of the 107 cases reviewed, nine were excluded from this study because of incomplete radiography or operative notes. In all patients obvious endocrine causes for infertility had been excluded and the patient's consort was shown to be fertile.

HSG was performed by the standard method used in this department.

TECHNIQUE

HSG was booked for a date within ten days of the onset of menstruation, but generally not less than

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seven days. The patients were premedicated with Tilidine Hydrochloride, 20 drops sublingually one hour before the procedure, and intravenous Hyoscine-N-Butylbromide, 20 mg at the commencement. After reassurance of the patient and using aseptic technique, the cervix was visualized using a speculum and clasped with Volsellum forceps. Either a screw type Leech Wilkinson, or Spackman's cannula was inserted into the endocervical canal.

Maintaining a seal between the cannula and cervical canal with gentle traction on the Volsellum and pressure on the cannula, water soluble contrast medium Meglumine Iodipamide 100% W/V (pre-warmed to 30°C), was injected slowly into the uterine cavity and fallopian tubes. Appearance of the uterine cavity and patency and mobility of the fallopian tubes was assessed by direct image intensification.

Radiographs included a supine control film before insertion of the cannula, single films during the phases of early uterine filling, tubal filling and peritoneal spill. For detection of minor deformities of the uterine cavity it was essential to obtain radiographs of the uterus in the true anteroposterior projection and this was achieved by cervical traction and oblique positioning of the patient where necessary. A radiograph was taken in the erect position 20 minutes after the completion of the procedure.

Occasional unwanted side effects of the procedure were colicky lower abdominal pain during injection of contrast, persistent lower abdominal pain for some hours after the procedure and cornual spasm. Rare complications were an exacerbation of dormant pelvic inflammatory disease, generalized peritonitis, venous or lymphatic intravasation or other manifestations of the systemic absorption of water soluble iodine containing contrast media. No anaphylactic reactions were seen in our series. Overall experience in our department has revealed a 3% incidence of pelvic infection after the procedure.

At laparotomy and laparoscopy (using double puncture technique) the uterus and fallopian tubes were visualized in their entirety, and patency of the fallopian tubes was demonstrated by prograde or retrograde injection of blue dye. Any point of obstruction could then be demonstrated by dilatation of the proximal tube or by the extent of blue staining.

Results and Interpretation

The results of the correlation between HSG and laparotomy or laparoscopy are summarized in Tables I and II.

Hydrosalpin

Hydrosalpinges were seen in 39% of the total number of fallopian tubes investigated. Agreement between HSG and operation was found in 70 of the 77 hydrosalpinges found at operation.

The radiological appearance was that of distal obstruction of the fallopian tube with dilatation of

TABLE I

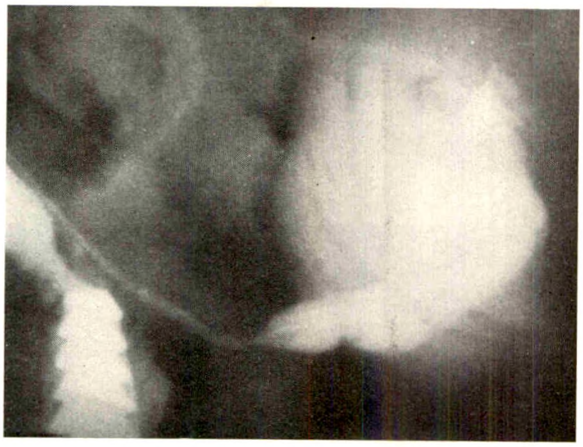
Tubal findings – 98 patients – (196 tubes)

Findings	Total		HSG diagnosis confirmed operatively	HSG diagnosis not confirmed operatively	Operative findings not diagnosed by HSG
	Single tubes	Percentage incidence			
Hydrosalpinx	77	39	70	0	7
Peritubal adhesions	127	65	123	5	4
Cornual spasm	6	3	6	0	0
Cornual obstruction	8	4	8	1	0
Isthmic obstruction	20	10	20	2	0
Distal obstruction	20	10	16	1	4
Normal fallopian tubes	18	9	16	5	2

TABLE II

Uterine findings – 98 patients

Findings	Total	HSG diagnosis confirmed operatively	HSG diagnosis not confirmed operatively	Operative findings not diagnosed on HSG
Leiomyomata	10	5	9	5
Congenital abnormalities	11	1	9	1



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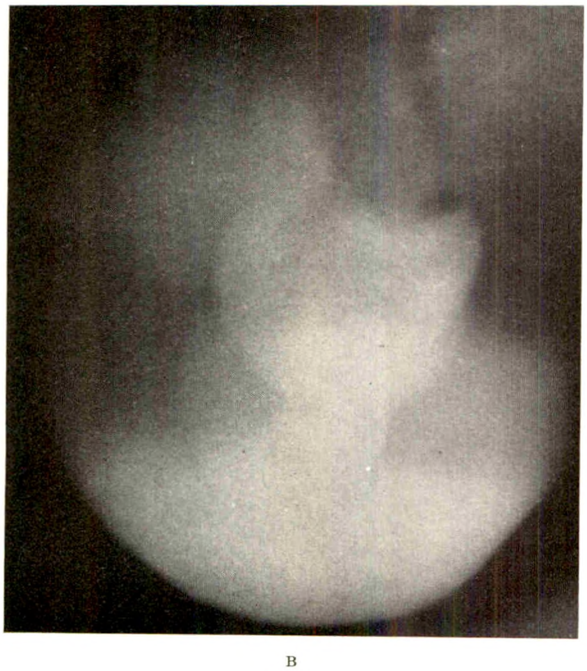

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Fig. 1.

(A) Hydrosalpinx. Ballooned obstructed terminal fallopian tube with fimbrial ridges.

(B) Hydrosalpinx. Twenty minute erect film showing fluid-contrast levels.

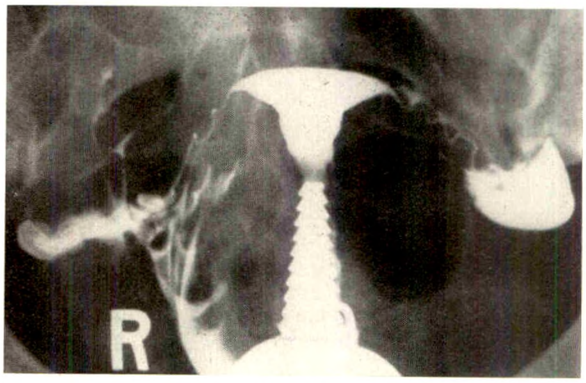

Fig. 2.

Adhesions-bilateral. Both tubes fixed, with isthmic and ampullary convolutions. Note undisplaced uterus.

the ampullary portion and obliteration of the normal internal mucosal architecture. There was free communication of the dilated area with the isthmic portion of the fallopian tube. The terminal ridges of adherent and ballooned fimbriae were sometimes visible. Fluid-contrast levels were frequently seen in the hydrosalpinx on the erect 20 minute radiograph (Fig. 1). Limited intraperitoneal spill of contrast material occasionally occurred on pressure separation of adherent fimbriae.

Peritubal adhesions

Sixty-five percent of the total number of fallopian tubes investigated showed evidence of peritubal adhesions. Agreement between HSG and operation was achieved in 123 of 127 fallopian tubes. Operation revealed adhesions in five further tubes reported as normal at HSG.

Multiple convolutions of the isthmus and ampulla of the fallopian tube, with reduced mobility which could be assessed on "push-up" and "pull-down" radiographs, or more conveniently by manipulation under fluoroscopy, were indicative of peritubal adhesions (Fig. 2). Lateral displacement of the uterus with fixity indicated peritubal adhesions only if associated with convolution and reduced mobility of the fallopian tubes (Fig. 3).

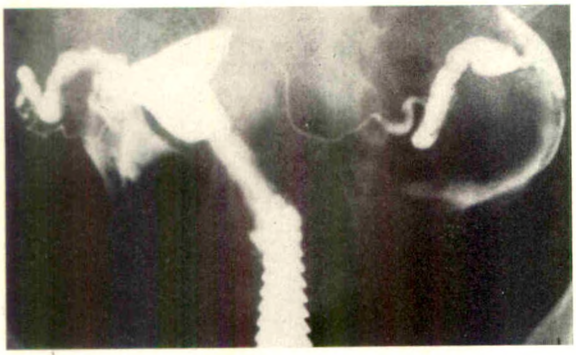

Fig. 3.

Adhesions-unilateral. Right tube fixed, with multiple convolutions of isthmus and ampulla. Uterus drawn to affected side.

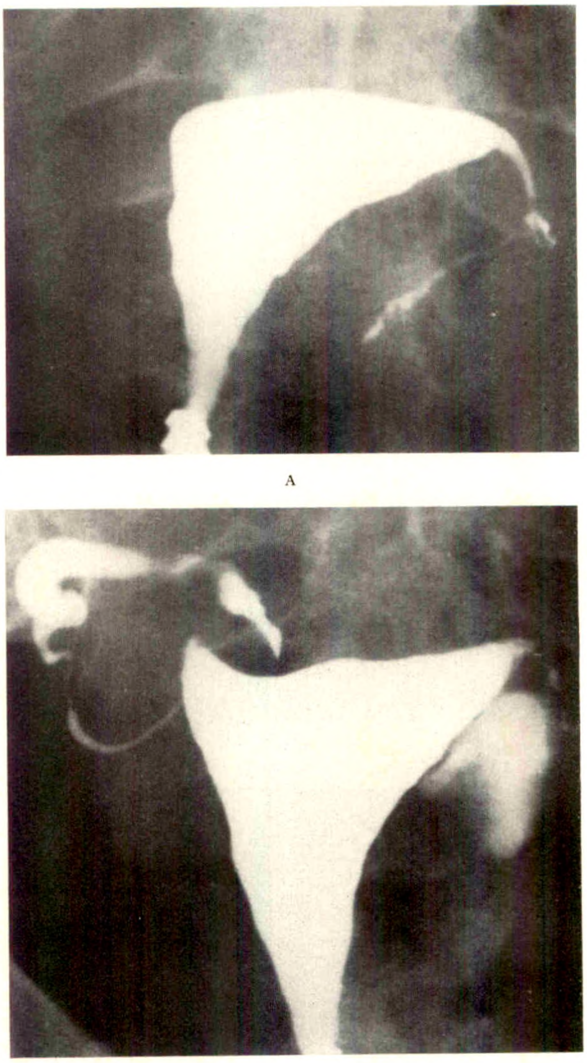

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Fig. 4.

(a) Right cornual spasm. Rounded cornual contour and non-filling of right tube.

(b) Relaxation of right cornual spasm after intravenous Hexoprenaline.

Cornual spasm

Persistent cornual spasm was identified in six fallopian tubes at HSG. Operative demonstration of patency of the tubes in these cases indirectly confirmed the radiological diagnosis of cornual spasm.

Spasm was characterized by a rounded "breast-like" cornual contour, which was either unilateral or bilateral (Craig, 1973; Sadek Foda *et al.*, 1962; Siegler, 1967b).

A useful adjunct to the diagnosis of cornual spasm is the intravenous injection of Hexoprenaline 10 mcg and the subsequent visualization of the fallopian tubes (Fig. 4). If this fails to demonstrate the fallopian tubes in apparent bilateral cornual spasm, and contrast is noted in the peritoneal cavity on the 20 minute radiograph, this is indirect evidence of spasm in at least one tube. The so-called "cornual sphincter" consists of a fold of mucous membrane, and does not constitute a sphincter mechanism (Schneider, 1942; Siegler, 1967b). If contrast is seen in the pretubal bulge, then there can be no cornual spasm and organic obstruction is diagnosed (Fig. 5).

Cornual occlusion

Of the eight fallopian tubes with cornual obstruction, all were accurately identified by HSG.

This was characterized by a pointed or irregular cornual margin (Sadek Foda *et al.*, 1962), and failure to visualize the fallopian tube after the administration of Hexoprenaline.

Partial distal occlusion of the fallopian tube without hydrosalpinx

Agreement between HSG and operation was found in 16 of the 20 fallopian tubes thus affected.

Some dilatation of the ampulla, retention of contrast in the ampulla at 20 minutes and late spill of contrast were indicative of partial occlusion of the fallopian tubes (Fig. 6). Lack of terminal dilatation and spill into the peritoneal cavity differentiated this from a hydrosalpinx.

Leiomyomata

Agreement between HSG and operation was found in five of the ten cases of leiomyomata.

Submucous leiomyomata presented hysterographically as well demarcated, rounded filling defects seen clearly during early filling of the uterine cavity. As filling continued, these defects became partially obscured by enveloping contrast (Kendall-Smith, 1975). Isthmic leiomyomata gave rise to retained contrast in the uterine cavity and fallopian tubes in two cases at 20 minutes, suggesting a "ball valve" mechanism (Fig. 7). Large intramural leiomyomata deformed the uterine cavity, and subserous leiomyomata were not possible to identify.

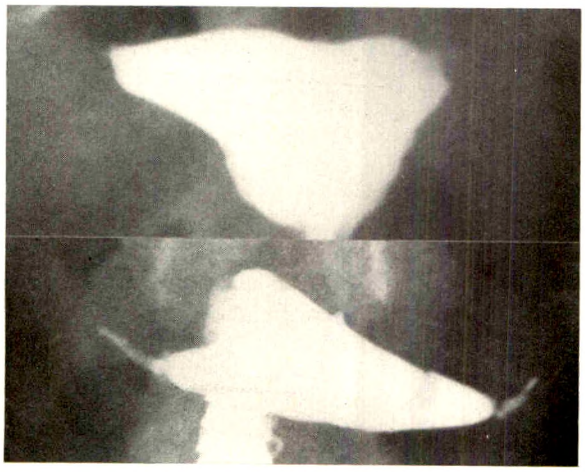

FIG. 5.

(Top) Bilateral cornual obstruction with irregular cornual contours.

(Bottom) Bilateral isthmic obstruction. Demonstration of "pretubal bulge" precludes cornual spasm.

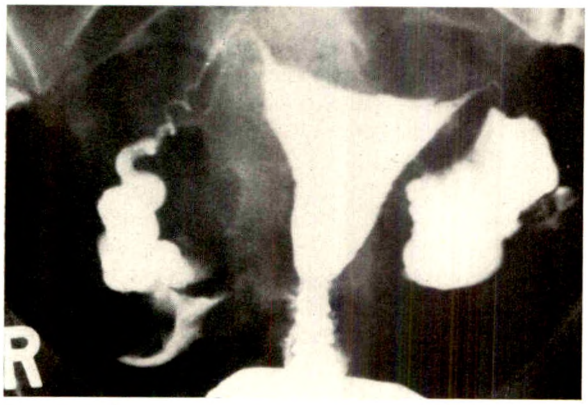

FIG. 6.

Partial distal occlusion of right fallopian tube. Evidence of bilateral adhesions and left hydrosalpinx.

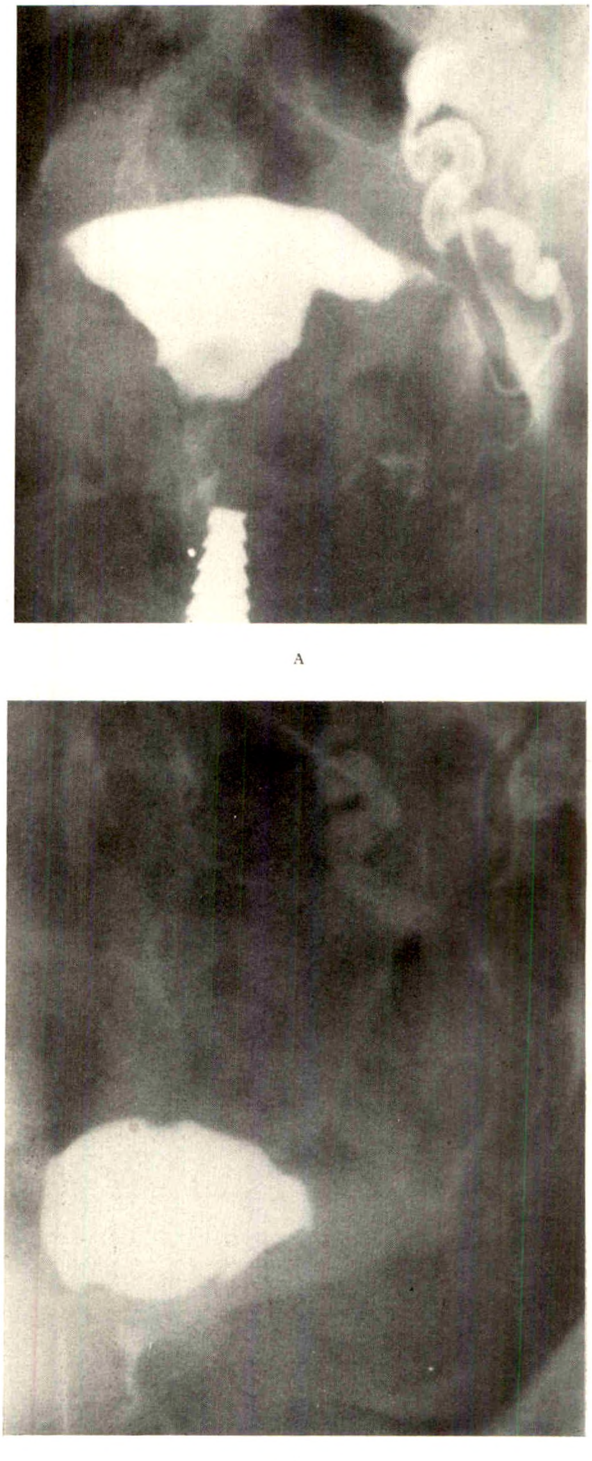

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FIG. 7.

(A) Isthmic submucous leiomyoma.

(B) Delayed film shows contrast retention in uterus and left fallopian tube.

Congenital uterine anomalies

In ten cases congenital anomalies of the uterus were diagnosed on HSG but only one of these was confirmed operatively. The majority were arcuate or subseptate uteri diagnosed according to the criteria and measurements of Tompkins (Craig, 1973; Tompkins, 1962).

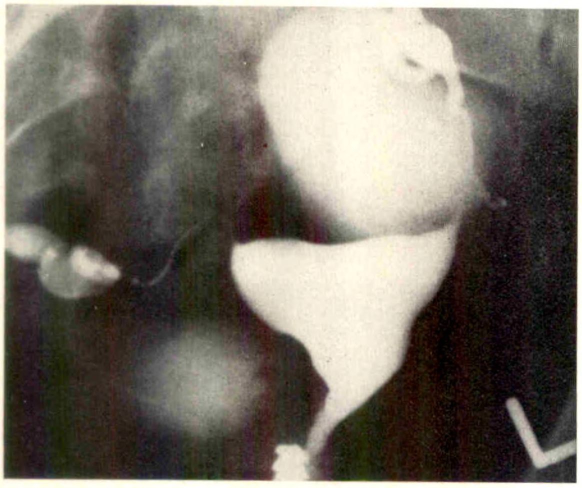
Discussion

The mechanical causes of female infertility, which can be radiologically elucidated, include hydrosalpinges and other tubal obstructions, peritubal adhesions, leiomyomata, congenital malformations of the uterus and intra-uterine synechiae. We have reviewed our material in an attempt to establish radiological criteria for the pathological processes encountered, and the accuracy with which each can be diagnosed.

Hydrosalpinx occurred in 39% of the total number of fallopian tubes investigated. This figure, associated with the high incidence of peritubal adhesions, indicates the prevalence of pelvic inflammatory disease in our group of patients. There were no unsubstantiated HSG diagnoses of hydrosalpinx, but a significant number of hydrosalpinges were detected only at operation. Technical difficulties at HSG accounted for the majority, with underfilling of the involved fallopian tube (Sweeney, 1962). This could have been due to the use of an inadequate volume of contrast material, or to the preferential flow of contrast into the opposite tube (Israel and March, 1976; Kierse and Vandervellen, 1973; Maathuis *et al.*, 1972). Contrast material will flow preferentially into the tube with a large hydrosalpinx, filling it at the expense of the contralateral side which may be similarly affected. To overcome this, a volume of contrast sufficient to fill both fallopian tubes is necessary. In addition, an erect delayed film at 20 minutes is mandatory (Fig. 8).

In two cases hydrosalpinges were not demonstrated because of proximal obstruction of the fallopian tubes. As our results demonstrate, with good technique a high accuracy can be anticipated in the diagnosis of hydrosalpinges.

The accurate diagnosis of peritubal adhesions is more difficult (Maathuis *et al.*, 1972; Moghissi and Gun Sup Sim, 1975). Underfilling of the fallopian tubes or proximal obstruction makes assessment impossible. It cannot be assumed that the pathological process always involves both sides, and a number of cases demonstrated unilateral peritubal adhesions. Discrepancies between radiological and operative findings could in some cases be attributed to a prolonged interval between the two investigations (Israel and March, 1976; Maathuis *et al.*, 1972). Intervening episodes of pelvic inflammatory disease may have altered the situation within that period. Multiple convolutions of the isthmus and ampulla are necessary for the diagnosis of peritubal adhesions. Convolution of the ampulla alone may be normal. In doubtful cases, where only ampullary convolution and fixity exist, laparoscopy will play an important role. Although our diagnostic accuracy was high, we feel that peritubal adhesions should be reported with caution.



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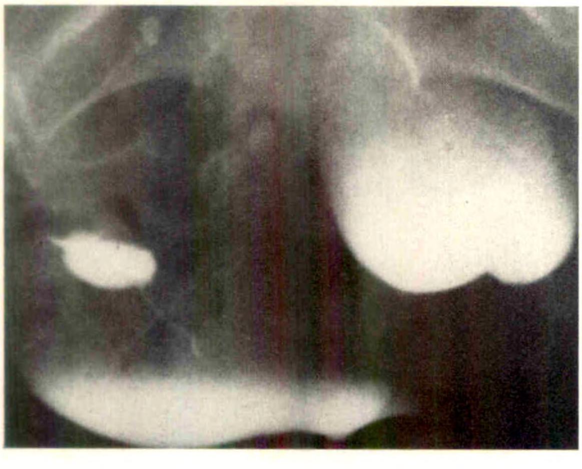

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Fig. 8.

(A) Large left hydrosalpinx with apparent early spill on right.

(B) Delayed film shows fluid-contrast level in huge right hydrosalpinx. No free intraperitoneal spill.

Loculated spill was not a valuable radiological sign, nor were perifimbrial adhesions without peritubal involvement possible to diagnose with accuracy.

Inaccuracies in the reporting of fallopian tubal obstructions were all due to under-filling of the affected tube for technical reasons, or to cornual spasm. It is necessary to differentiate between distal obstruction and hydrosalpinx as, by definition, hydrosalpinx implies dilatation of the ampullary portion with thinning of adherent fimbriae and destruction of mucosa. A distal obstruction may occur without these features and may be incomplete, allowing some spill of contrast material, whereas the hydrosalpinx is closed and can spill only by pressure separation of fimbriae.

Retention of contrast material in a fallopian tube 20 minutes after removing the cannula from the cervix is often regarded as evidence of obstruction or internal mucosal destruction. However, retention occured in two patients in our series with normal fallopian tubes. In both, large submucous isthmic leiomyomata were present and retention may have been on the basis of a "ball valve" effect, preventing drainage from the uterine cavity and fallopian tubes.

By applying the criteria mentioned, cornual spasm should not be confused with cornual obstruction. At HSG, cornual spasm was diagnosed in six fallopian tubes which proved to be patent at operation, thus confirming the hysterographic diagnosis.

Submucous leiomyomata were accurately demonstrated on the basis of the appearance described, but the intramural or subserous types proved more difficult to diagnose. With obvious deformity of the uterine cavity by a large intramural fibroid the diagnosis can be made with more confidence. The concept of the "bulky" uterus with enlarged uterine cavity proved to be inaccurate, accounting for all our false positive reports, and we feel that this concept should be discarded.

Minor degrees of arcuate or subseptate uterus demonstrated at HSG may appear externally normal on direct vision (Craig, 1973). This was borne out by our experience, and these borderline cases accounted for our high incidence of positive reports of congenital anomalies of the uterus not confirmed by operation. We consider the HSG in this instance to be more accurate than laparoscopy or laparotomy.

The Leech-Wilkinson cannula used in association with Volsellum forceps on the cervix, has proved satisfactory. It allows ease of application, watertight fit between cannula and endocervix, and important structures are not obscured by the long tip found in other cannulae. When the Leech-Wilkinson cannot be applied due to tears or other malformations of the cervix, the Spackman or Provis cannulae have usually proved successful. Sedation and analgesia are essential during what is an emotionally disturbing and sometimes painful procedure. General anaesthesia is not required and would be an unnecessary risk. A quiet, relaxed atmosphere in the examination room and reassurance of the patient are important factors in the prevention of cornual spasm.

Extratubal pathology, such as enlarged ovaries or masses could not be diagnosed with any accuracy and some of the "ovaries" reported in our series were probably loops of bowel outlined by peritoneal spill of contrast. Pelvic endometriosis was discovered operatively in only three patients, reflecting the low local incidence. No characteristic radiological features could be determined, apart from the presence of peritubal adhesions in every case.

CONCLUSION

The gynaecologist requires information as to the extent of the functional and mechanical impairment of the fallopian tubes and uterus. An accurate impression of mechanical impairment can usually be provided by HSG alone, but this does not always correlate with the degree of functional impairment caused by peritubal adhesions preventing normal tubal motility. In view of the accepted risk of operation, we feel that the decision to allow a trial period before ordering laparoscopy, or proceeding directly to laparotomy, can be made on the basis of the findings on HSG.

In the light of the accuracy of our results, it should be possible to report on an HSG with an evaluation of the probable accuracy of the findings. If the radiologist is confident of his diagnosis, laparoscopy will only be indicated where cornual obstruction is demonstrated, or to confirm the extent of pelvic disease in cases where further surgery will probably be of no benefit. The remainder will be managed conservatively or will undergo laparotomy. Where doubt exists, as in the case of possible peritubal adhesions without other abnormality, or in apparently normal HSG where the patient has not become pregnant within a year of investigation, laparoscopy will be indicated. This protocol will save much time and expense in a busy unit, by the avoidance of unnecessary diagnostic laparoscopies.

In the approach to the investigation and the management of female infertility hysterosalpingography plays a primary role, and the radiologist remains an important member of the infertility team.

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REFERENCES

Annual Report, Obstetrics and Gynaecology Department, Groote Schuur Hospital, 1976.

Coltart, T. M., 1970. Laparoscopy in the diagnosis of tubal patency. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, *77*, 69–71.

Craig, C. S. J., 1973. Congenital abnormalities of the uterus and foetal wastage. *South African Medical Journal*, *47*, 2000–2005.

Frangenheim, H., 1967. Vergleichende untersuching en zwischen dem wert der hysterosalpingographie und der coelioskopie bei der sterilitätsdiagnostik. *Archiv für Gynäkologie*, *204*, 167–168.

Gabos, P., 1976. A comparison of hysterosalpingography and endoscopy in evaluation of tubal function in infertile women. *Fertility and Sterility*, *27*, *3*, 238–242.

Israel, R., and March, C. M., 1976. Diagnostic laparoscopy: a prognostic aid in the surgical management of infertility. *American Journal of Obstetrics and Gynaecology*, *125*, *7*, 969–974.

Kendall-Smith, I. M., 1975. Space occupying lesions of the uterus at hysterography. *Australasian Radiology*, *XIX*, *4*, 338–343.

Kierse, M., and Vandervellen, R., 1973. A comparison of hysterosalpingography and laparoscopy in the investigation of infertility. *Obstetrics and Gynaecology*, *41*, *5*, 685–688.

Maathuis, J. B., Horbach, M. D., and Hall E. V. E., 1972. A comparison of the results of hysterosalpingography and laparoscopy in the diagnosis of fallopian tube dysfunction. *Fertility and Sterility*, *23*, *6*, 428–431.

Moghissi, K. S., and Gun Sup Sim., 1975. Correlation between hysterosalpingography and pelvic endoscopy for the evaluation of tubal factor. *Fertility and Sterility*, *26*, *12*, 1178–1181.

Sadek Foda, M., Abdel Fattah Youssef, Shafeek, M. A., and Kassem, K. A., 1962. Hysterography in diagnosis of abnormalities of the uterus. III. Acquired abnormalities (continued). *British Journal of Radiology*, *35*, 836–842.

Schneider, P., 1942. The problem of the tubal sphincter and of the intramural portion of the fallopian tube. *American Journal of Roentgenology*, *48*, *4*, 527–542.

Siegler, A. M., 1967a. Dangers of hysterosalpingography. *Obstetrical and Gynaecological Survey*, *22*, 284–308.

Siegler, A. M., 1967b. *Hysterosalpingography*. Harper and Row, New York.

Sweeney, W. J., 1962. Pitfalls in present day methods of evaluating tubal function. II – Hystersalpingography. *Fertility and Sterility*, *13*, *2*, 124–134.

Tompkins, P., 1962. Comments on the bicornuate uterus and twinning. *Surgical Clinics of North America*, *42*, *4*, 1049–1062.

Book review

Diagnostic Ultrasound in Clinical Obstetrics and Gynecology. By H. E. Thompson and R. J. Bernstine, pp. xii+192, illus., 1978 (John Wiley & Sons Ltd., Chichester, Sussex), £17·65.
ISBN 0-471-86080-8.

This small book is one of the recent wave of ultrasound texts. The purpose of the book is to "help the clinician use ultrasound without involving unnecessary engineering and physical details". However, although approximately 100 pages are devoted to obstetrical ultrasound, only 25 pages are devoted to gynaecological ultrasound, and the remainder of the book contains a brief description of the mechanics, system and basic technique. In such a small text a relatively comprehensive description of the mechanics and systems available seems somewhat superfluous, in view of the numerous texts already available.

The section on obstetrics is lucidly written and contains much useful basic information. The section on gynaecological ultrasound seems a little dated. This is demonstrated by the references given at the end of the chapters, few of which are later than 1975. This may be a reflection of the time taken from preparation to final production, but a number of recent papers have demonstrated the increased accuracy of ultrasound in the demonstration and differentiation of adnexal masses. Similarly, the section on pelvic malignancy is somewhat brief. The quality of the images in the book is reasonable, but a further complaint shared in common with recent texts, is the number of bistable images present, which would be better omitted, however unusual the condition. In all, this is an informative book of basic obstetrical and gynaecological ultrasound. One hopes that a further edition will expand and update the gynaecological content at the expense of the physical aspects, which will make this an extremely useful little book.

C. H. Wright.

1979, *British Journal of Radiology*, *52*, 263–267 APRIL 1979

The radiological diagnosis of polyps in the presence of diverticular disease

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ABSTRACT

The double contrast barium enemas in 20 patients with endoscopically proven polyps within a segment of diverticular disease have been reviewed. Ninety per cent of the polyps were detected. The increased density sign and negative shadow filling defect proved valuable in their detection. Antispasmodics are advised to distend the sigmoid and allow double contrast views to be obtained. With severe diverticular changes it may be impossible to exclude a polyp, and if the patient complains of rectal bleeding, endoscopy is indicated.

The detection of colonic polyps poses a complex problem in the presence of diverticular disease. The difficulty is accentuated where there is severe muscle thickening (Berenbaum and Berenbaum, 1965). Colonoscopy has shown that the double contrast barium enema is capable of diagnosing polyps of over 5 mm diameter with an accuracy of 95%. However, failure to detect a polyp radiologically is most likely to occur in the sigmoid in association with diverticular disease (Williams *et al.*, 1974). The radiological problems in diagnosing polyps in the presence of diverticular disease are discussed, and criteria suggested for their diagnosis.

MATERIALS AND METHODS

The double contrast barium enemas of 20 patients with colonic polyps and diverticular disease were examined. In 19 the presence of polyps had been established endoscopically, and in one following resection. The cases were selected to include only those where polyps had been found endoscopically within a segment of diverticular disease. The ages of the patients ranged from 40 to 80 years. Nine were female and 11 male.

The radiographs were viewed by the two authors in conjunction, without knowledge of the endoscopic findings, as to the site of the polyp. The following criteria were used to distinguish a polyp from a diverticulum, and to detect the presence of a polyp with a segment of diverticular disease (Fig. 1). When both are viewed tangentially there is obviously no difficulty in distinguishing a polyp from a diverticulum. The problem arises when either are viewed *en face* or at an angle.

Radiographic signs of a polyp

1. The base of a sessile polyp seen in double contrast will either show as an elipse or two concave lines (Young, 1969). Barium covering the surface of the dome of the polyp forms the "bowler hat sign" (Youker and Welin, 1965).
2. A penduncalated polyp seen in double contrast *en face* shows as a target sign, the outer ring being due to barium covering the head of the polyp, the inner ring from barium around the stalk (Young 1969).
3. A pedunculated polyp viewed obliquely in double contrast will show the stalk as two parallel or slightly converging lines in the lumen of the bowel, leading to the head of the polyp. The presence of two such lines is referred to as the "stalk sign" (Fig. 2).
4. Sessile or pedunculated polyps by virtue of being intraluminal lesions cause an "increased density sign" when seen in double contrast (Fig. 3). This is due to two factors. First, the soft tissue mass of the lesion in the lumen reduces the air that the beam travels through, so that there is increased attenuation. Second, barium covering the polyp and the mucosa results in greater attenuation as the beam has to traverse four layers of barium. This does not apply to a divericulum seen *en face* in double contrast as only two layers of barium are traversed, corresponding to normal bowel, and the distance through air is increased so that attenuation may actually be reduced (Fig. 4).
5. The region of the polyp may not be seen in double contrast. The polyp may be shown as a negative shadow as it is a filling defect in the barium (Fig. 5) (Youker and Welin, 1965).

Requests for reprints to C. I. Bartram.

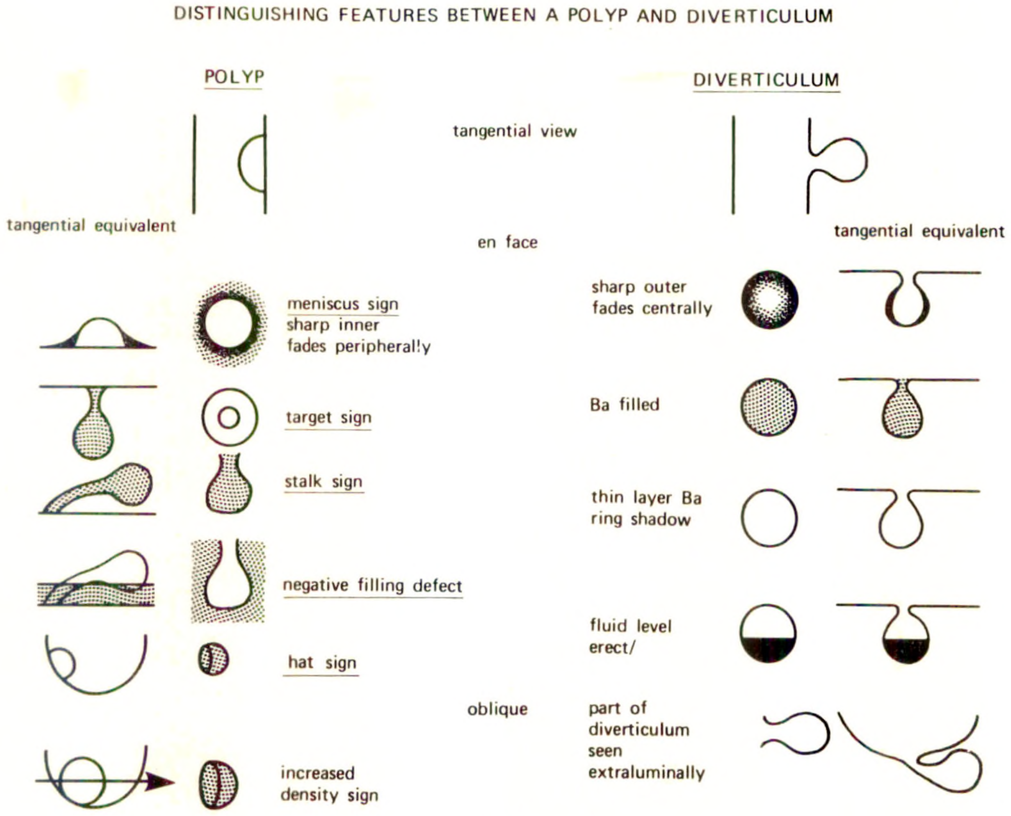
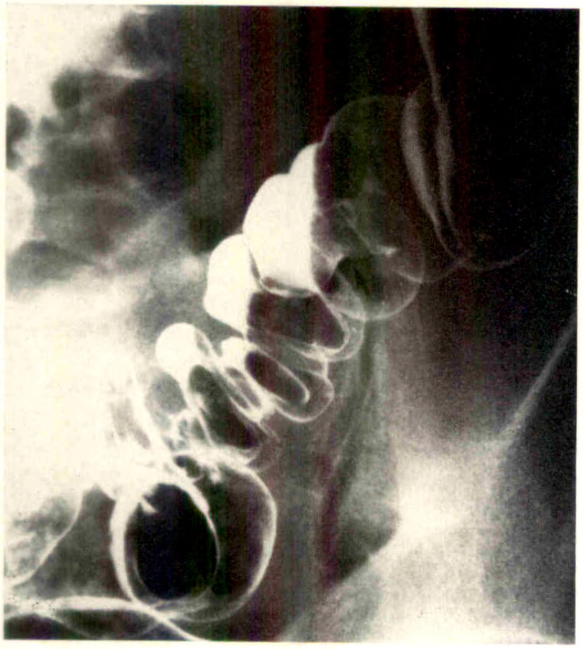


FIG. 1.
Distinguishing features between a polyp and diverticulum.



Radiographic signs of a diverticulum seen en face

1. The diverticulum may fill completely with barium (Fig. 4).
2. If partly filled with barium the "meniscus sign" may be apparent. The outer border of the barium is smooth and even as it lines the diverticulum. The meniscus fades centrally. With a polyp the inner part of the ring is smooth as it surrounds the base of the polyp, and the meniscus fades peripherally (Youker and Welin, 1965).
3. In decubitus or erect views a diverticulum partially filled with barium will show a fluid level.
4. If a diverticulum contains only a thin layer of barium this will produce a ring shadow (Fig. 4). but there is no increased density, target, stalk or hat sign.

RESULTS

Polyps were not seen in two patients. In one patient there was gross diverticular disease in the

FIG. 2.
Stalk sign. Parallel lines of the pedicle (arrow) leading to the head of the polyp which is obscured by a pool of barium.

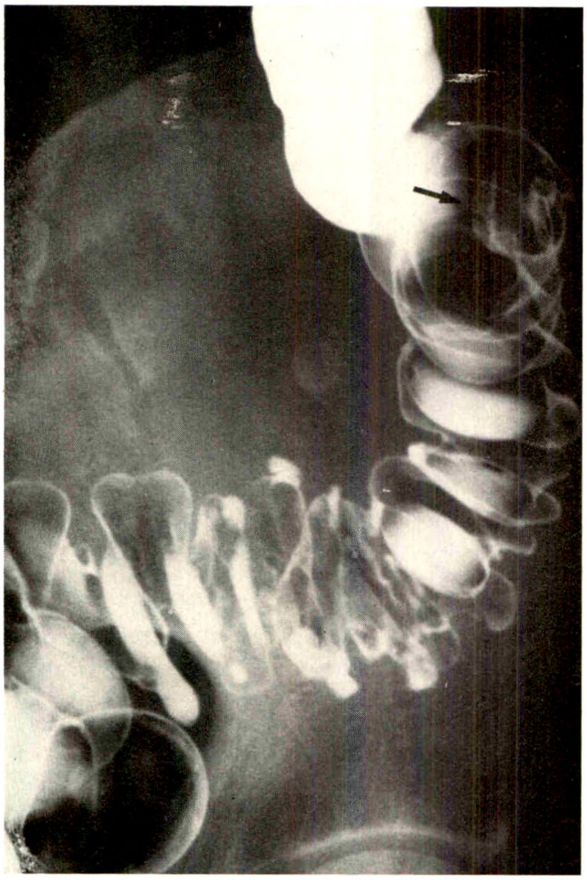


FIG. 3.
Sessile polyp showing up as an intraluminal lesion of increased density (arrow).

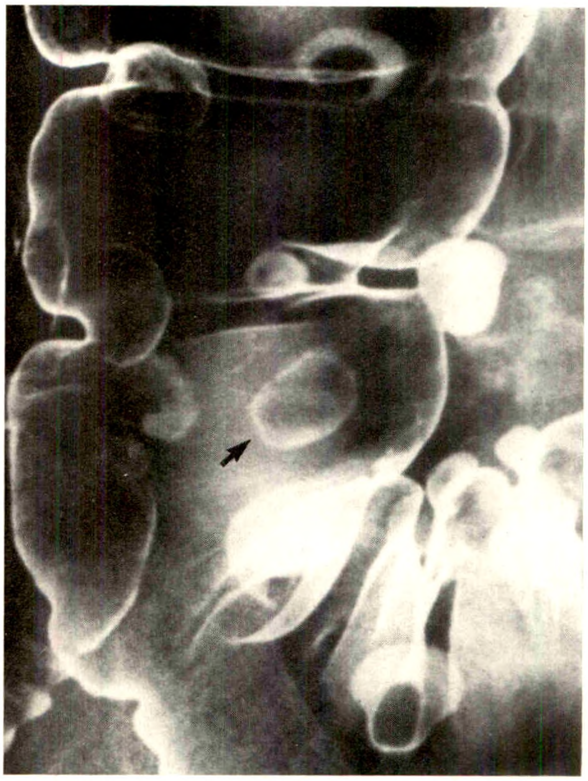


FIG. 4.
En face view of diverticulum lined by a thin layer of barium (arrow). No increase in density. Some diverticula are partially or completely barium filled.

sigmoid with considerable muscle deformity. The lumen could not be clearly identified (Fig. 6). The resected specimen is shown in Fig. 7. In the other patient the sigmoid loops were superimposed and not shown in double contrast. Two polyps, 7 and 2 mm in diameter were missed.

In the 18 patients in whom polyps were detected, the signs described were elicited in the following frequency:
Increased density of the polyp —14;
Filling defect with negative shadow —10;
Meniscus sign —9;
Stalk sign —7;
Hat sign —3;
Target sign —2;

Eighteen polyps were found: eight were pedunculated. The largest polyp detected in the series was

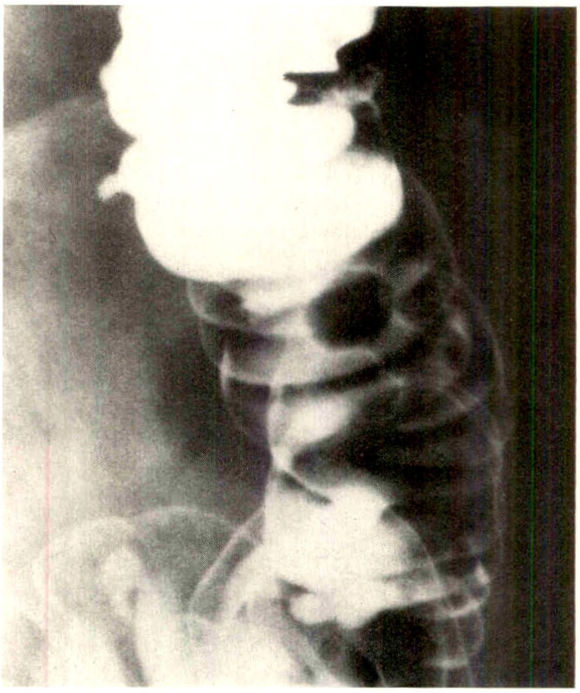


FIG. 5.
Pedunculated polyp seen as a negative filling shadow.

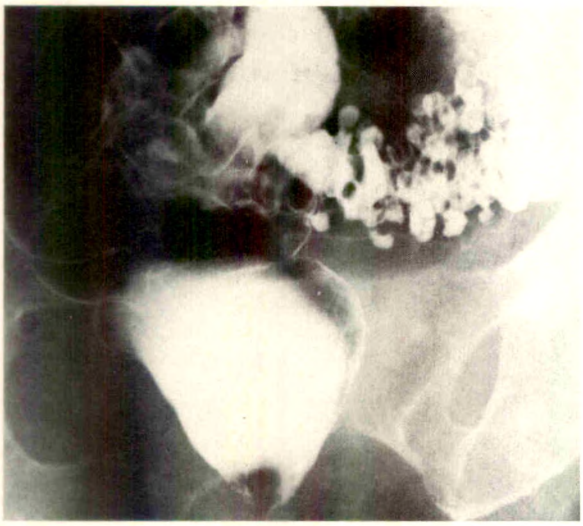


FIG. 6.

Gross diverticular disease. Lumen not defined. No polyp diagnosed radiologically.

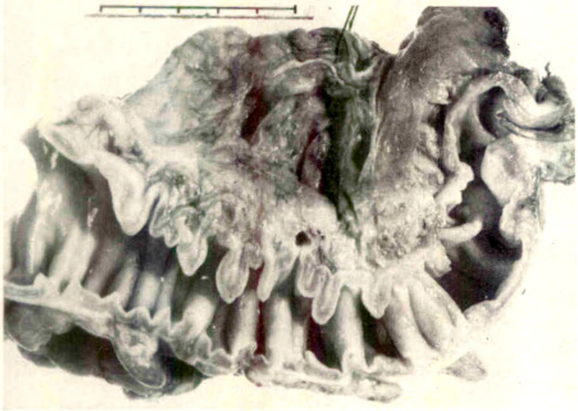


FIG. 7.

Resected specimen showing pedunculated polyp (arrow).

4.5 cm in diameter, the smallest 8 mm. In three cases four different signs of a polyp were elicited, and in three only one sign. In three patients the polyp was seen in double contrast only in one view, and completely obscured by barium in all other views. Utilizing the described signs, a diverticulum was not confused with a polyp in any case.

DISCUSSION

Adenomatous polyps are common in the sigmoid colon in older patients (Arminski and McLean, 1964). Diverticular disease is also common in this age group, being present in almost half of the population over 50 years of age (Hughes, 1969). The diverticula are commonest in the sigmoid (Zollinger, 1968), which is also where the muscle abnormality predominates (Morson, 1963). It is therefore to be expected that these two lesions should frequently coexist. Radiologically this presents several problems.

The sigmoid colon is the most difficult part of the large bowel to demonstrate on barium enema. It is liable to be obscured by overlapping loops of redundant colon, or small bowel if barium has refluxed into the terminal ileum. Barium also tends to pool in the sigmoid loop. The standard double contrast barium enema views may therefore reveal only parts of the sigmoid colon in double contrast, in one or two projections. This is reflected in the number of occasions when a polyp was seen as a negative filling defect in the barium, and that in three patients the polyp was only visible in one view.

It is therefore important to ensure that optimum double contrast views of the sigmoid are obtained. Technically this may be achieved by adequate drainage of the rectum prior to air insufflation, then rotation of the patient from left lateral to prone, to right lateral during air insufflation, so that the barium is driven as a column out of the distal colon towards the caecum. Antispasmodics are particularly helpful when muscle thickening is present. Greater distension is possible which reduces the muscle deformity thereby lessening pooling of barium between interdigitating folds. Reflux of barium into the terminal ileum is prevented by completing air insufflation in the prone position, when the ileo-caecal valve is non-dependant so that air only will reflux.

The presence of diverticula undoubtably detracts from the ease of polyp detection (Fig. 6). Spotting a stalk or area of increased density (Figs. 2 and 3) often provides the initial clue to the presence of a polyp, which can then be fully delineated on closer inspection.

Careful examination of the sigmoid colon is necessary in the presence of diverticular disease. However, in spite of all precautions it may be impossible to detect a polyp. This is of considerable importance in patients with colo-rectal bleeding. Bleeding should not be attributed solely to the presence of diverticular disease. If no polyp is found the patient should still be referred for colonoscopy (Williams *et al.*, 1974), which will often reveal an adenomatous polyp.

REFERENCES

ARMINSKI, T. C. and MCLEAN, D. W., 1964. Incidence and distribution of adenomatous polyps of the colon and rectum based on 1000 autopsy examinations. *Diseases of the Colon and Rectum*, 7, 249–261.

BERENBAUM, L. and BERENBAUM E. R., 1965. Small polypoid lesions associated with spastic diverticulosis. *Diseases of the Colon and Rectum*, 8, 78–84.

HUGHES, L. E., 1969. Postmortem survey of diverticular disease of the colon. *Gut, 10*, 336–344.

MORSON, B. C., 1963. The muscle abnormality in diverticular disease of the colon. *British Journal of Radiology, 36*, 385–392.

WILLIAMS, C. B., HUNT, R. H., LOOSE, H., RIDDELL, R. H., SAKAI, Y. and SWARBRICK, E. T., 1974. Colonsocopy in the management of colonic polyps. *British Journal of Surgery, 61*, 673–682.

YOUKER, J. E. and WELIN S., 1965. Differentiation of true polypoid tumours of the colon from extraneous material: a new roentgen sign. *Radiology, 84*, 610–615.

YOUNG, A. C., 1969. *Diseases of the colon, rectum and anus.* pp. 38–61 (W. Heinemann).

ZOLLINGER, R. W., 1968. The prognosis of diverticulitis of the colon. *Archives of Surgery, 97*, 418–422.

Book review

Management of Primary Bone and Soft Tissue Tumors. pp. xii+474, illust., 1977 (Year Book Medical Publishers, Inc. Chicago, London), £31·00.

This volume reports 35 papers presented at the 21st Annual Clinical Conference on Cancer held at the M. D. Anderson Hospital and Tumor Institute, Houston, Texas in 1976, 27 of these being entirely or mainly based on experience at this well-known centre. To assess progress in knowledge and management of sarcomas during 13 years one may compare this book with the similar volume of approximately equal size published in 1965 (No.2 of this present series). Relatively less space is now devoted to histopathology, with a significant increase in the amount about chemotherapy and tumour immunology. Unavoidably, this book is already outdated, since many clinical trials detailed were ongoing so that preliminary results only were available. Nevertheless, the large volume of information, both on diagnosis and management, will be rewarding to the general reader and can be amplified by the sarcoma specialist by reference to the journals.

With so many authors some inequality of style and value of papers is inevitable, but a high standard of clarity is maintained throughout, although some topics have been compressed or over-simplified in the interests of brevity. With minor exceptions the illustrations are good, and the numerous diagrams and tables clear and precise.

Many diagnostic problems are considered, starting with the histopathology of several less common types of soft tissue sarcomas, including the recently described tumour resembling Ewing's sarcoma of bone. Histological grading of tumours and its correlation with prognosis receives considerable attention, but one wonders to what extent such evaluation of histological structure would be reproducible by reviewing pathologists. Sarcoma staging and its bearing upon the selection of appropriate therapy is reported, with comments about several pseudosarcomatous lesions and that presently-popular neoplasm—malignant fibrous histiocytoma.

An unusually interesting paper recounts metabolic studies of young osteosarcoma patients, relating the findings to the prevalence of this tumour during the period of active skeletal growth. It is a pity that anthropometric data of the patients were not included in the tables, other than the Tanner stage of sexual development. In an otherwise excellent review of classification of primary bone tumours a curious statement appears concerning giant cell tumours of bone—"The better differentiated lesions have a stroma that is histologically malignant" (p.71); in the writer's experience this is quite incorrect. The value of diagnostic electron microscopy is discussed with special reference to Ewing's tumour of bone and certain soft tissue sarcomas.

The surgical section provides good coverage of biopsy methods and the basic principles of surgical management. It is refreshing to note round condemnation of the archaic procedure of "shelling-out" a tumour. The danger of wound contamination by minute invisible tumour fragments is mentioned, but not sufficiently emphasized. For benign and less aggressive bone tumours wide excision or resection, if needful with prosthetic sequence, is advocated in preference to curettage and grafting with its attendant risks of local recurrence. To a pathologist it is disappointing that more emphasis is not laid upon the prime objective of biopsy—the provision of adequate material for pathological diagnosis (a point which still eludes some less experienced operators).

Work on the frequency of intra-osseous "skip" metastases has been extended, but without any very firm conclusions about their importance in deciding the level of ablation of a limb involved by osteosarcoma. Two further papers report methods of clinical staging of patients with bone or soft tissue tumours, giving analyses of the results. Although elaborate, such detailed information seems an essential component of a well conducted clinical trial. Two papers deal with combined treatment by preoperative radiotherapy for soft tissue sarcomas and conservative surgery followed by irradiation of these tumours.

This leads on naturally to radiotherapy alone or combined with chemotherapy for osteosarcoma and soft tissue tumours, with a report on the trial of chemotherapy for rhabdomyosarcoma. Now well into the realm of the bold-face acronym, there is a great deal more about trials of various protocols for soft tissue sarcomas and preoperative intra-arterial chemotherapy with simultaneous irradiation, which is claimed to increase soft-tissue tumour necrosis above the level achieved by irradiation alone.

Fifty pages relate the intricacies of tumour immunology and its therapeutic exploitation, either alone or combined with other treatment.

Two papers follow on neurosurgery for severe intractable pain and on the surgical removal of lung metastases, the latter closing on an encouraging note of patients thus rescued. Lastly, a clinico-pathological conference discusses eight soft tissue lesions, illustrating some diagnostic problems.

This book provides a mass of "hard" facts, and also a considerable measure that are not so hard. On the whole it merits careful reading, and is a valuable addition to the library of the clinician or pathologist dealing with bone or soft tissue sarcomas.

A competent subject index and adequate bibliography are provided.

C. H. G. PRICE.

1979, *British Journal of Radiology*, *52*, 268–272

Magnification renal arteriography

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Abstract

Magnification selective renal arteriograms were performed on 24 patients, 12 of whom were hypertensive, and compared with non-magnification arteriograms by two observers independently.

The magnification angiograms were performed on a Siemens Microfocus Bi 125/3/50 RG tube with a 0.1 mm focal spot.

Of the 24 patients examined, information crucial to the diagnosis was found only on the magnification films in three patients (12.5%). Extra information compared with the non-magnification films was found in the magnification films in 12 patients (50%). No additional information was discovered in the remaining nine patients (37.5%). The magnification angiograms enabled the interlobular vessels to be visualized—this was not possible on the non-magnification films.

Against the additional information gained must be weighed the disadvantages of magnification arteriography which include increased radiation dose and lengthening of procedure time plus additional injections of contrast.

In conclusion, there is a place for magnification renal arteriography and the advantages seem to outweigh the disadvantages.

Extraction of the maximum possible information from a renal arteriogram is every radiologist's aim especially with regard to the modern potential for microvascular surgery (Clunie *et al.*, 1975). Other reasons for wanting an accurate delineation of the small vessels of the kidney are studying the earliest stages of rejection, and assessing hypertension and pyelonephritis (Sidaway, 1972). Several surveys have been published on the use of magnification renal arteriography in humans (Greenspan *et al.*, 1967; Sidaway 1972; Casarella 1973; Stein 1973; Cope *et al.*, 1974) and dogs (Sherwood *et al.*, 1969), but these have been with a 0.3 mm focus tube. The use of the 0.1 mm focus spot tube has been reported, but only with reference to skeletal radiography (Genant *et al.*, 1977). It now seems timely to assess renal magnification arteriography using the 0.1 mm focal spot.

Of the 24 patients, 13 were male and 11 were female. Their ages varied from 16 years to 79 years (mean 48.7 years).

Materials and Methods

On each of the 24 patients a midstream aortic injection was performed (by the Seldinger technique) using 50 ml of Conray 325 (sodium iothalamate). Bilateral selective renal injections were then performed (except, of course, in the patient with a unilateral absent kidney). For each selective injection 8 ml of Conray 280 (meglumine iothalamate) were injected by hand. Magnification angiograms were then performed with 8 ml of Conray 280, also being injected by hand.

The X-ray tube that was used for all the examinations was a Siemens Microfocus Bi 125/3/50 RG. For all the angiograms an AOT changer was used with Cronex 4 AOT film.

The selective (non-magnification) angiograms were performed with a 1 mm focal spot tube using factors of 77 kV, 13 mAs (0.025 sec exposure). These factors are an approximation and were varied for each patient.

The magnification angiograms were performed with 0.1 mm focal spot. Other factors used for the magnification angiograms were 3.2 mAs, 100 kV (0.1 sec exposure). These factors were also adjusted to suit the individual patient.

On the first two patients the 0.2 mm focal spot was used but when it was found that the 0.1 mm focus could be used all the remaining angiograms were performed with the 0.1 mm focus.

For the magnification angiograms the focus to film distance was 120 cm and the focus to subject distance was 60 cm giving a 2 to 1 magnification. With the non-magnification angiograms, films were taken at the rate of two per second for the first six seconds and then one per second for four seconds. With the magnification films, only three exposures were taken at a rate of one per second as this was the maximum that the rating of the tube would allow without overloading.

All the films were examined independently by two radiologists and it was decided which films gave more information. The films which gave more information were scored + and the other films 0. If both films gave equal information both were scored 0.

Results

Out of 24 patients examined, information crucial to the diagnosis was found on the magnification films only in three patients (12.5%). Extra information compared with that found on non-magnified films was found in another 12 patients (50%). No additional information was discovered in the remaining nine patients (37.5%). The results are summarized in Table I.

Of the three cases in which crucial diagnostic information was found, one was a case where unequivocal fibro-muscular hyperplasia had been shown in the right renal artery (Fig.1) and appearances highly suggestive of fibro-muscular hyperplasia were shown on the left (Fig. 2A). The magnification films show conclusively that there is no fibro-muscular hyperplasia on the left but that the appearances were due to a combination of vessel branching and wave effect (Fig. 2B). While it is appreciated that a repeat non-magnification run may have demonstrated the wave effect, it could not have differentiated conclusively the vessel branching from the suspected fibro-muscular hyperplasia.

TABLE I

Clinical diagnosis and helpfulness of radiographs

Age	Sex	Diagnosis	Non-Magnification	Magnification
33	M	Hypertension, right renal artery stenosis	0	+
39	F	Hypertension	0	+
59	F	Carcinoma right kidney	0	+
24	F	Hypertension	0	+
52	M	Hypertension	0	0
41	M	Hypertension, left renal artery stenosis	0	+
47	F	Hypertension, fibro-muscular hyperplasia right renal artery	0	+
49	M	Hypertension	0	0
79	M	Left renal cyst	0	0
56	F	Hypertension	0	+
48	M	L Hydronephrosis, haematuria	0	0
16	M	Absent kidney	0	+
39	M	Hypertension	0	+
48	M	Right pyelonephritis, haematuria	0	+
47	F	Hypertension	0	+
42	F	Hypertension	0	0
64	M	? left renal mass—normal	0	0
58	F	Right renal cyst	+	0
53	M	Right pyelonephritis, haematuria	0	+
65	M	Carcinoma left kidney	0	+
23	F	Right renal artery stenosis	0	0
62	F	Bilateral pyelonephritis	0	0
51	M	Renal donor	0	+
72	F	Carcinoma right kidney	0	+

+ = More helpful; 0 = less helpful,
If both scored 0 = Equal information from both sets of films.

The second case was one where an undisputed 1 cm long tight stenosis was visualized at the origin of the right renal artery with post-stenotic dilatation (Fig. 3A). What is not apparent on the non-magnification films is that there is a second tight stenosis near the origin of one of the branches to the lower pole of the right renal artery and this was only clearly seen on the magnification films (Fig. 3B). In the third case, a suspected fibro-muscular hyperplasia on the non-magnified films was shown to be merely a tortuous vessel on the magnification films.

Of the 12 patients where extra information was gleaned from the magnification angiograms, five had

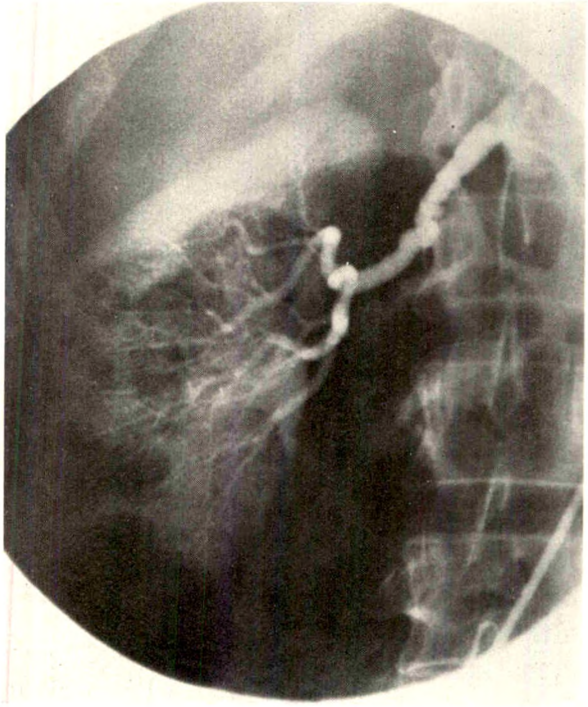

Fig. 1.

Non-magnification film. Fibro-muscular hyperplasia of right renal artery.

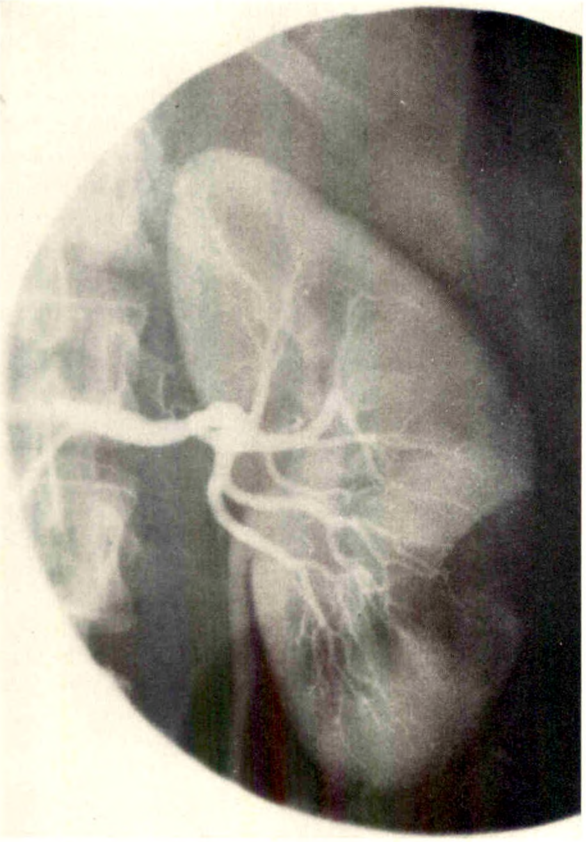

FIG. 2A.

Non-magnification film. Apparent fibro-muscular hyperplasia of left renal artery.

hypertension, three had a renal tumour, two had unilateral pyelonephritis with haematuria, one had a unilateral absent kidney and one was a renal donor.

In the five hypertensive patients, magnification angiograms permitted visualization of interlobular arteries which were not adequately visualized on the non-magnification films. In all five patients the interlobular arteries were shown to be more tortuous and irregular with abnormal branching (Fig. 4A and 4B) compared with the other patients in the series who were not hypertensive (Ljungquist, 1962). Better visualization of the interlobar and arcuate vessels was also achieved in these patients and a similar increase in tortuosity and irregularity was shown in these vessels.

We did not feel that accurate glomerulography was possible with our technique although glomerular columns were visualized on some of the films (Cope *et al.*, 1974).

Of the seven other patients with improved visualization on magnification angiography, one had a renal tumour. On the venous phase it was apparent that not only was the renal vein invaded (seen on the non-magnification films) but that the tumour had spread outwith the wall of the renal vein, which was not apparent on the non-magnified films. With regard to the further six patients, one had a unilateral absent kidney, and magnification angiography showed the interlobular vessels on the contralateral side (normal) which were not seen in the non-magnification films. Another two patients had haematuria and unilateral pyelonephritis—the magnification angiograms showed that the interlobular vessels were abnormal with variations in calibre and loss of normal pattern. The non-magnification films did not permit visualization of these changes. Of the remaining three patients in this group, two had renal carcinoma and the magnification films gave more accurate delineation of the tumour boundaries by virtue of better visualization of tumour circulation at the periphery of the tumour. In the sixth patient of

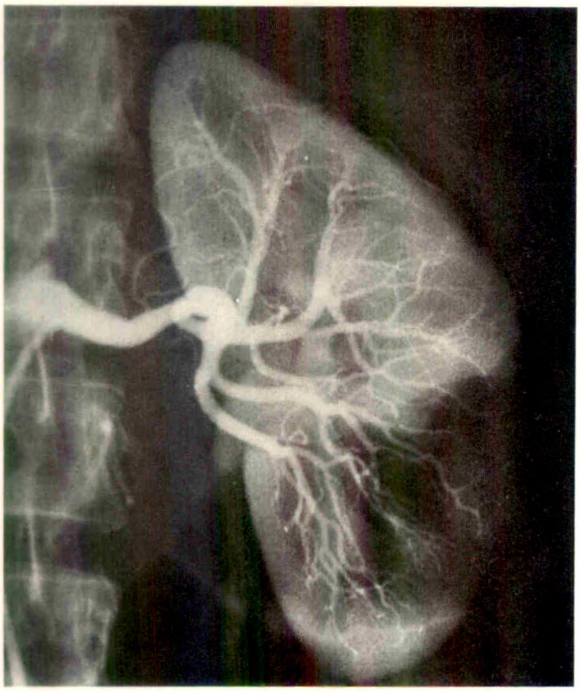

FIG. 2B.

Magnification film. No fibro-muscular hyperplasia. Appearances due to a combination of "wave" effect and vessel branching.

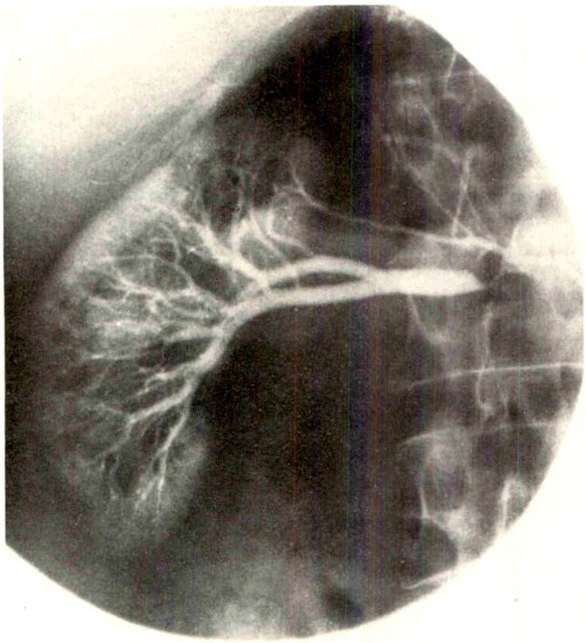

FIG. 3A.

Non-magnification film. Right renal artery stenosis with post stenotic dilatation.

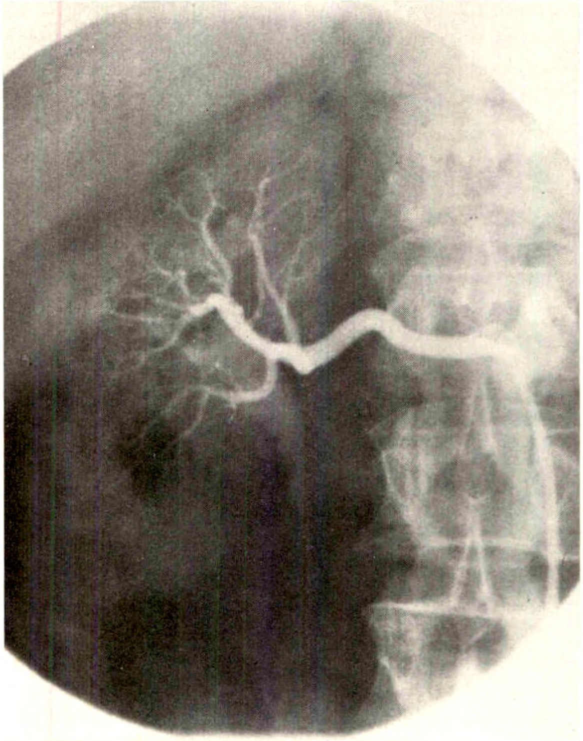

FIG. 4A.

Non-magnification film. Patient with essential hypertension. Interlobular arteries not visualized.

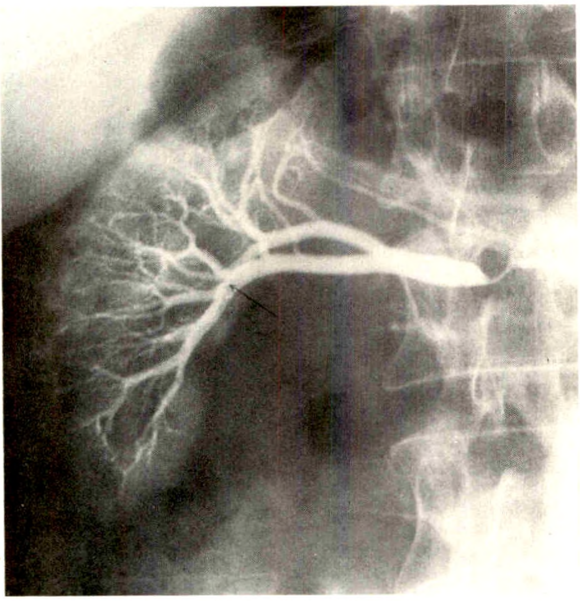

FIG. 3B.

Magnification film. Second stenosis visible in intra-renal branch artery.

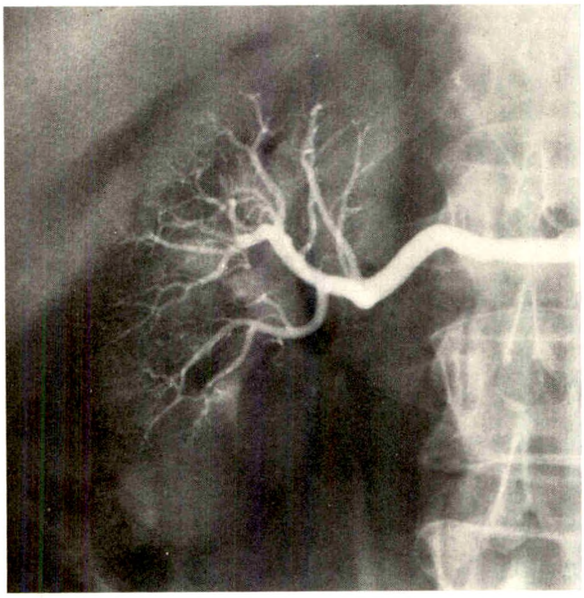

FIG. 4B.

Magnification film. Same patient as Fig. 4A. Interlobular arteries visualized showing abnormal branching pattern, tortuosity and irregularity.

this group, the renal donor, the magnification films showed the arcuate and interlobular arteries which were not visualized on the non-magnification films.

In the remaining nine cases no additional information was obtained on the magnification radiographs, and in fact in one patient less information was obtained due to movement blur.

It was felt that the two sets of angiograms taken on the 0.2 mm focus were subjectively as good as those taken with the 0.1 mm focus but the number is too small to draw any conclusions.

Correlation between observers was good with 92% agreement as to assessment.

Discussion

Times two magnification renal angiography gave increased information in 62.5% of patients, was of no additional value in the remaining 37.5% and in fact gave reduced information in one patient (4%). These figures do not reach statistical significance but show a promising trend and suggest the need for a larger trial which is under way. The disadvantages are increased radiation dose and lengthening of procedure time plus additional injections of contrast.

With our present equipment we found it was not possible to obtain satisfactory images at 3 to 1 magnification, and 2 to 1 magnification was the best that we could obtain during renal angiography, although 4 to 1 magnification gives good results with extremities, using our equipment. The increased exposure time with magnification technique leads to more movement blur than normal but the high kV technique reduces this greatly.

A drawback in our system is that at present we are only able to expose a series of three films at one film per second due to tube rating, and therefore matching up an equivalent phase film of a magnification and non-magnification run to give a true comparison can be difficult. The variability in pressure of the hand injections was probably not a significant factor. There is an increased quantum mottle effect with magnification technique and this reduces image quality.

In conclusion, there seems to be a place for magnification renal angiography. We believe the increased information gained outweighs the disadvantages enumerated above.

Acknowledgments

The authors wish to express thanks to Dr. E. Barnett and Dr. F. G. Adams who performed some of the angiograms and to Miss J. O. S. McDermid, Superintendent Radiographer, Western Infirmary, Glasgow.

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REFERENCES

Casarella, W. J., 1973. Latest advances in diagnostic urologic radiology 1. Magnification renal arteriography. *Urology*, *1*, 501–505.

Cope, C., Raja, R. M. and Isard, H. J., 1974. Correlation of glomerulography and renal function in hypertension. *Radiology*, *110*, 15–19.

Clunie, G. J. A., Gordon, R. D. Hartley, L. C. J., Petrie, J. J. B., and Hardie, I. R. 1975. Results of surgical treatment of renovascular hypertension. *Medical Journal of Australia*, *1*, 225–228.

Genant, H. K., Doi, K. K., Mall, J. C., and Sickles, E. A. 1977. Direct radiographic magnification for skeletal radiology. *Radiology*, *123*, 47–55.

Greenspan, R. H., Simon, A. L., Ricketts, H. J., Rojas, R. H., and Watson, J. C. 1967. *In vivo* magnification angiography. *Investigative Radiology*, *2*, 419–431.

Ljungquist, A., 1962. The intra-renal arterial pattern in essential hypertension. A micro-angiographic and histologic study. *Journal of Pathology and Bacteriology*, *84*, 313–325.

Sherwood, T., Lavender, J. P., Greenspan, R. H., 1969. Renal magnification angiograms in the dog. Observations in responses to vasodilators and surgical trauma. *British Journal of Radiology*, *42*, 241–246.

Sidaway, M. E., 1972. Small vessel changes in renal disease. *British Medical Bulletin*, *28*, 247–249.

Stein, H. L., 1973. Direct serial magnification renal arteriography: a clinical study. *Journal of Urology*, *109*, 967–970.

Book review

Atlas of Carotid Angiography. Edited by M. Takahashi, pp. xvii+525, illus., 1977 (Igaku Shoin Ltd, Tokyo), £46·80.

The atlas presents a balanced selection of good quality subtraction prints illustrating the diagnostic scope of carotid angiography.

The text is brief, but it gives an adequate description of the methods and a good discussion of normal anatomy and its variants. Sections devoted to pathological appearances also discuss the main angiographic abnormalities and are supplemented by a well selected bibliography, but the work is obviously not intended to replace the more comprehensive textbooks.

The atlas should be useful for reference at all stages of training, but would be especially valuable to those commencing study of neuroradiology.

B. E. Kendall.

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Angiography in leiomyosarcoma of the inferior vena cava—report of two cases

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ABSTRACT

Two patients with leiomyosarcoma of the suprarenal inferior vena cava are presented. In one case the tumour was misinterpreted as intrahepatic at angiography. In the second case an extrahepatic location was suggested after repeated angiography. The diagnosis should be borne in mind when a large hypovascular mass appears to be located centrally in the liver at coeliac angiography and when ultrasound examination has revealed its solid nature.

Leiomyosarcoma of vascular origin is a rare tumour. The majority of these tumours arise from veins, predominantly the inferior vena cava (Szasz *et al.*, 1969, Kevorkian and Cento, 1973; Bailey *et al.*, 1976; Stitz and Boulter, 1976). Angiographic findings in leiomyosarcoma of the IVC have been described only in a few cases (Wray and Dawkins, 1971; Couinaud, 1973; Justiniani *et al.*, 1973; Stuart and Baker, 1973; Brewster *et al.*, 1976; Tegtmeyer and Buschi, 1977; Schildberg and Kuntz, 1977).

The angiographic findings of another two patients will be presented in this report and the difficulties in differentiating extra- from the intrahepatic tumours at angiography will be discussed. One case (case 1) has previously been described in brief (Granmayeh *et al.*, 1978).

REPORT OF CASES

Case 1

A 71-year-old white female was admitted with three months' history of epigastric pain. On physical examination a large mass was palpated in the epigastrium. Barium examination of the stomach and duodenum revealed forward dislocation of the stomach. Liver scintigraphy demonstrated a tumour in the left lobe of the liver and a subsequent biopsy suggested an haemangioma. At coeliac and hepatic angiography (Fig.1) a large hypovascular mass was found dislocating the left lobe of the liver. A few irregular branches from the hepatic artery were identified. Lumbar aortography did not reveal any vascular supply to the tumour, which was felt to be located in the liver.

At laparatomy the tumour was found to originate from the IVC at the level of the renal veins. There was no involvement of the liver or surrounding organs, and the tumour and an omental implant could be removed. The tumour protruded into the lumen of the IVC, which was opened and cleaned of tumour and clots. The postoperative course was uneventful. Microscopic examination of the tumour and the omental implant showed a well differentiated leiomyosarcoma. Postoperative irradiation of 4500 rad was given. Two-and-a-half years later the patient had physical signs of liver metastases. No further follow-up is available.

Case 2

A 73-year-old white female was admitted with three months' history of abdominal distension and epigastric pain. A large mass was palpated in the epigastrium. Barium examination of the stomach and duodenum revealed dislocation of the stomach but no tumour infiltration. Cholecystography, ERCP and colon examination were normal. Ultrasound examination of the abdomen demonstrated a huge solid tumour, probably located in the liver involving the right and the left lobe. Liver scintigraphy revealed an enlarged liver with decreased uptake in the hilum. A fine needle aspiration biopsy was performed giving a diagnosis of sarcoma. Lumbar aortography did not reveal any tumour vascularity. Angiography of the coeliac and superior mesenteric artery was performed. A large hypovascular mass considered to originate from the left medial segment separating this from the left lateral segments and compressing the

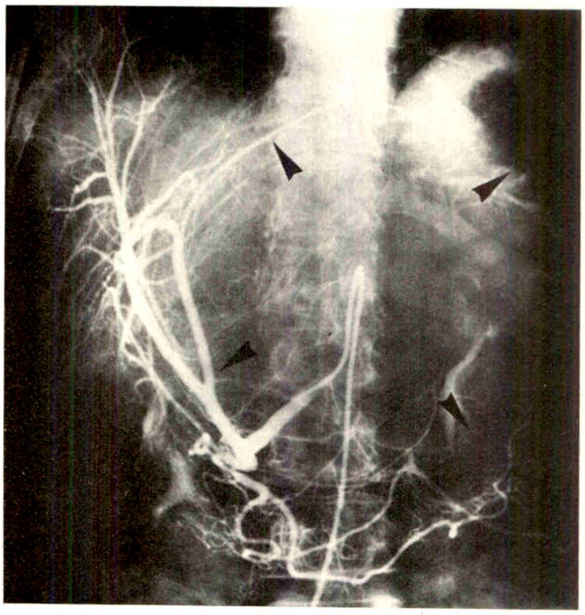


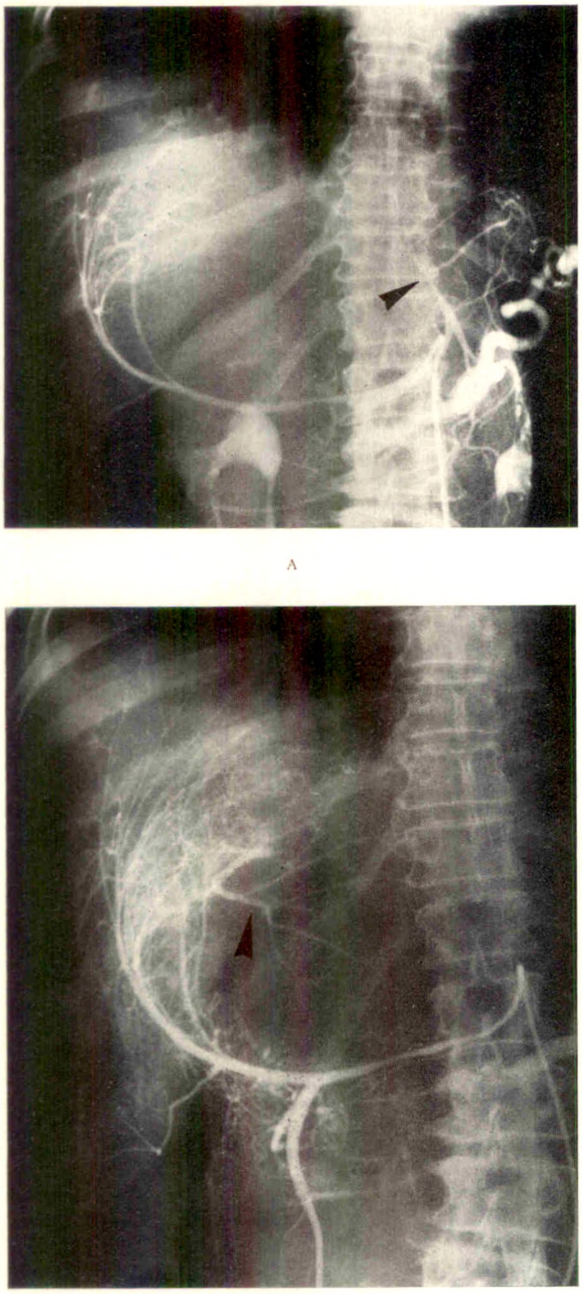
Fig. 1. *Case 1.*

Hepatic angiography. Large hypovascular mass (▲) dislocating the common hepatic artery inferiorly, the right hepatic arteries to the right and left hepatic arteries superiorly and to the right. (Reprinted with permission from *American Journal of Roentgenology*).

Address reprint requests to U. Nyman.

right lobe was demonstrated (Fig.2A). Vessels believed to represent tumour vascularity were found in the right lobe. Because of these findings the tumour was regarded unresectable.

The patient was later referred for intra-arterial chemotherapy and it was then possible to catheterize the narrowed hepatic artery. At angiography of the hepatic artery with infusion technique (40 ml; 3 ml/sec) more adequate filling of the hepatic artery and its branches was achieved (Fig. 2B). It was then obvious that the tumour did not separate the left lateral segment from the rest of the liver but compressed the left lobe as well as the right lobe. Intra-arterial chemotherapy was given three times with two weeks interval with 50 mg of adriamycin each time. No clinical effect of the therapy was noticed. It was then suggested that the tumour might be located outside the liver compressing the parenchyma. Laparotomy was performed and the tumour was found to arise from the suprarenal part of the IVC. The liver was compressed by the tumour but was otherwise normal. A small protrusion of the tumour into the lumen of the IVC was identified, but there was no thrombus or obstruction. The tumour, weighing 3.5 kg, could be removed leaving just a small part adherent to the IVC. No attempts were made to resect and reconstruct the IVC in order to remove all tumour tissue in this old patient. Microscopy revealed a well differentiated leiomyosarcoma. Post-operative irradiation of 6000 rad was given and the patient is well six months after surgery.



A

B

Fig. 2. *Case 2.*

(A) Coeliac angiography. Large hypovascular mass dislocating the stretched and narrowed common hepatic artery inferiorly and right hepatic arteries to the right. The arteries indicated by arrowhead were misinterpreted as left hepatic arteries simulating separation of the left lobe of the liver from the right by an intrahepatic mass.

(B) Hepatic infusion angiography. Contrast filling of the left hepatic artery (▲). Irregular hepatic arteries and contrast accumulation in the right lobe representing compressed parenchyma.

COMMENTS

The vascularity of leiomyosarcoma differ depending on the site of origin. Small bowel lesions are hypervascular, and enlarged feeding arteries and early draining veins may be demonstrated, while retroperitoneal leiomyosarcomas generally are hypo- to moderately vascular (Levin *et al.*, 1973; Granmayeh *et al.*, 1978). In the retroperitoneum these tumours get their main arterial supply from lumbar arteries, and depending on the extent of the disease also from the coeliac, the superior and inferior mesenteric, or the renal arteries. Retroperitoneal leiomyosarcomas are generally large at the time of diagnosis thus causing distortion of major arteries and veins, and adjacent organs. Angiography in both our cases demonstrated large poorly vascularized tumours compressing the liver parenchyma with stretching and dislocation of the common hepatic artery anteriorly and inferiorly. A similar angiographic finding regarding leiomyosarcoma of the IVC has been described in reports by Couinaud (1973), Stuart and Baker (1973), and Schildberg and Kuntz (1977), while hypervascular tumours occurred in cases reported by Wray and Dawkins (1971), Justiniani *et al.*, (1973), Brewster *et al.*, (1976), and Tegtmeyer and Buschi (1977). In all the cases with hypervascular lesions the hepatic arteries supplied the tumour. At surgery or autopsy these tumours invaded the liver or extended into the hepatic veins in all but one case (Brewster *et al.*, 1976) where no details about the extension of the tumour was given.

Leiomyosarcomas of the IVC most frequently occur at the level between the renal veins and the diaphragm and since their arterial supply may be derived from hepatic arteries, these tumours may easily be misinterpreted as liver tumours at angiography. In our first case the tumour erronously was thought to be located in the liver. In case 2 an extrahepatic location of the mass was suggested after selective hepatic infusion angiography when the vascular anatomy could be better appreciated, and from the experience of case 1. In most published cases, where a cavography has been performed an obstruction of the IVC was present. This is, however, of no differential diagnostic help since large liver tumours may compress the IVC without any overgrowth to the vein.

According to Rossi and Ruzicka (1969), abnormal vessels arising from the hepatic arteries, distortion of hepatic artery branches, radiolucency within the liver during the parenchymal phase and extension of hepatic arteries to the periphery of the liver are angiographic findings that should be considered when making a distinction between intra- and extra-hepatic masses. These findings were not sufficient in our cases to make this distinction and the same was found by Shanser *et al.* (1974). Their clue for making a diagnosis of an extrahepatic mass was the angiographic finding of stretched and attenuated intrahepatic arteries, without superior and inferior arcing around the mass and without irregularity of these arteries. This sign was of no help either in our cases. The intrahepatic arteries were stretched around the mass and what was initially thought to represent tumour vascularity was probably caused by impaired circulation in compressed parenchyma.

To reveal the true extrahepatic nature of these tumours the plane of cleavage between the liver and the tumour must be determined. This may be obtained by oblique or lateral views at angiography. Ultrasound examination may demonstrate the relationship between the liver and the mass, but was of no help in this respect in one of our cases. Computerized tomography adds a new dimension and may help to solve the problem.

In retrospect an extrahepatic location of the tumour should have been suspected in both cases since such a large hypovascular mass rarely occurs in the liver. Primary tumours are generally more vascular and hypovascular metastases are in most instances smaller and multiple. A cyst may grow very large but is usually then surrounded by a rim of opacified parenchyma (Rizk *et al.*, 1971; Neiman and Goldstein, 1975) and furthermore ultrasound in our case 2 revealed a solid mass.

CONCLUSION

Leiomyosarcoma of the IVC is a rare tumour and may easily be misinterpreted as an intrahepatic mass at angiography. This tumour should, however, be borne in mind, when the combination of a large hypovascular mass in the upper part of the abdomen demonstrated at coeliac angiography and ultra-sonic evidence of its solid nature is present; especially in women over the age of 40, where it most frequently occurs. Vascular supply from branches of the hepatic artery indicates infiltration of the liver or extension into hepatic veins and a non-resectable lesion.

REFERENCES

Bailey, R. V., Stribling, J., Weitzner, S., and Hardy, J. D., 1976. Leiomyosarcoma of the inferior vena cava. Report of a case and review of the literature. *Annals of Surgery*, *184*, 169–173.

Brewster, D. C., Athanasoulis, C. A., and Darling, R. C. 1976. Leiomyosarcoma of the inferior vena cava. Diagnosis and surgical management. *Archives of surgery*, *111*, 1081–1085.

Couinaud, C., 1973. Tumeurs de la veine cava inférieure. *Journal de Chirurgie, Paris*, *105*, 411–432.

Granmayeh, M., Jonsson, K., McFarland, W., and Wallace, S., 1978. Angiography of abdominal leiomyosarcoma. *American Journal of Roentgenology*, *130*, 725–730.

Justiniani, F. R., Cohen, G. H., Roen, S. A., Arribas, I., and Kushner, D. S., 1973. Budd-Chiari syndrome due to leiomyosarcoma of the inferior vena cava. *Digestive Diseases*, *18*, 337–346.

Kevorkian, J., and Cento, D. P., 1973. Leiomyosarcoma of large arteries and veins. *Surgery*, *73*, 390–400.

Levin, D. C., Watson, R. C., and Baltaxe, H. A., 1973. Arteriography of retroperitoneal masses. *Radiology*, *108*, 543–551.

Neiman, H. L., and Goldstein, H. M., 1975. Angiography of benign and malignant hepatic mass. *Seminars in Roentgenology*, *10*, 197–205.

Rizk, G. K., Tayyarah, K. A., and Ghandur-Mnaymneh, L., 1971. The angiographic changes in hydatid cysts of the liver and spleen. *Radiology*, *99*, 303–309.

Rossi, P., and Ruzickz, F. F., 1969. Differentiation of intrahepatic and extrahepatic masses by arteriography. *Radiology*, *93*, 771–780.

Schildberg, F. W., and Kuntz, R. M., 1977. Leiomyosarkome der vena cava inferior. *Thoraxchirurgie*, *25*, 28–35.

Shanser, J. D., Glickman, M. G., and Palubinskas, A. J., 1974. Pitfalls in the arteriographic differentiation of intrahepatic and extrahepatic masses. *American Journal of Roentgenology*, *121*, 420–429.

Stitz, R. W., and Boulter, P. S., 1976. Leiomyosarcoma of the venous wall. *Clinical Oncology*, *2*, 163–171.

Stuart, F. P., and Baker, W. H., 1973. Palliative surgery for leiomyosarcoma of the inferior vena cava. *Annals of Surgery*, *177*, 237–239.

Szasz, L. J., Barr, R., and Scobie, T. K., 1969. Leiomyosarcoma arising from veins: two cases and a review of the literature on venous neoplasms. *Canadian Journal of Surgery*, *12*, 415–419.

Tegtmeyer, C. J., and Buschi, A., 1977. The angiographic diagnosis of leiomyosarcoma of the inferior vena cava. *Radiology*, *122*, 683–685.

Wray, R. C., Jr., and Dawkins, H., 1971. Primary smooth muscle tumors of the inferior vena cava. *Annals of Surgery*, *174*, 1009–1018.

1979, *British Journal of Radiology*, 52, 276–280

Ultrasound in the evaluation and diagnosis of jaundice

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ABSTRACT

Our experience in the evaluation and diagnosis of jaundice by ultrasound in a consecutive series of patients examined in the past year is reported. A final diagnosis is available in 49 patients with obstructive jaundice and 41 patients with non-obstructive jaundice. The accuracy of separation into these two groups is 97% in this series. We would like to stress the value of ultrasound as a complete investigation in many jaundiced patients. In this series a full diagnosis of the cause of jaundice was achieved in 58% of patients.

In the past few years the ultrasound diagnosis of obstructive jaundice has been shown to be accurate in experienced hands. The positive diagnosis of extrahepatic obstruction approaches 100% (Taylor *et al.*, 1974; Conrad *et al.*, 1978; Malini and Sabel, 1977). The basis for making the diagnosis is the identification of a dilated biliary tree in the jaundiced patient. We report our experience over a twelve-month period in which a series of 111 consecutive patients presenting with jaundice were examined. We would like to emphasize the value of ultrasound imaging not only as a screening procedure to separate obstructive jaundice from other causes of jaundice but in the accurate specific diagnosis of jaundice in many instances.

SUBJECTS AND METHODS

It has become the practice in our hospital for most jaundiced patients to have an ultrasound examination as soon as possible after presenting. Over a twelve-month period a series of 111 consecutive patients have been examined. All patients had a bilirubin level greater than 3 mg% (50 milliosmoles/litre). A final diagnosis is available in 90 patients, obtained by review of the patients' records. In all patients shown to have obstructive jaundice the final diagnosis was reached at laparotomy or in a few instances at post mortem. Biopsy results are available in most patients with non-obstructive jaundice. However, six patients with infective hepatitis have been included without biopsy proof, as in these instances the biochemical studies, auto-immune studies and clinical course were so typical for there to be no reasonable doubt as to the diagnosis. Twenty-one cases had to be excluded where proof of diagnosis was not available (refusal of biopsy, laparotomy or post mortem). All examinations were performed using a commercially available grey-scale unit and a 2.25 MHz 19 mm long internally focused transducer. Initially a series of longitudinal and transverse scans were done at 2 cm intervals using the standard single sweep technique, where possible in suspended inspiration. Transverse oblique scans were taken to maximize pancreatic visualization. In all cases of obstructive jaundice it is our practice to rotate the patient 30 deg into the right anterior oblique position to maximize visualization of the full length of the common bile duct, with a series of closely spaced longitudinal scans. A common bile duct measurement of over 8 mm by ultrasound was considered dilated (Behan and Kazam, 1978). This technique has proved particularly valuable in demonstrating both the level and cause of obstruction. The left lateral position may occasionally be of value in demonstrating the lower end of the common bile duct. This position is also used for intercostal scans when the liver is obscured by bowel gas in other positions. In these circumstances only limited views of the liver parenchyma may be obtained, however this is often sufficient to confirm or exclude obstruction as a cause of jaundice.

In all cases with no evidence of obstruction initially we now make a positive search for the main left and right hepatic ducts lying adjacent to the portal veins. Even when of normal calibre these are quite frequently demonstrated (Fig. 1).

RESULTS

In the full series of 111 patients there were two scan failures due to excessive bowel gas. This failure rate of 2% is surprisingly low. The possible explanation for this lies in the fact that many jaundiced patients have enlarged livers which are more easily demonstrated and also in the value of intercostal scans in the left lateral position. Although for most other situations a fairly comprehensive view of the liver is required for a successful study in the patient with obstructive jaundice, limited views of the liver will often be adequate to confirm the presence of dilated ducts.

A positive final diagnosis is available in 90 patients, 49 of whom had obstructive jaundice and 41 non-obstructive jaundice. Details are given in Tables I

TABLE I

OBSTRUCTIVE JAUNDICE

Diagnosis	Patients	Ultrasound diagnostic	Ultrasound helpful	Ultrasound failed
Carcinoma of the pancreas	18	12(66%)	1(6%)	—
Stones in common bile duct	19	11(58%)	5(26%)	3
Carcinoma of gall-bladder	1	—	1	—
Cholangiocarcinoma and infiltrating lesions at porta hepatis	3	3(100%)	—	—
Ampullary carcinoma	3	2(66%)	1(33%)	—
Non-malignant stricture CBD	3	—	3(100%)	—
Dilated CBD – no stones found	2	1(50%)	1(50%)	—
Totals	49	29(59%)	12(24%)	3

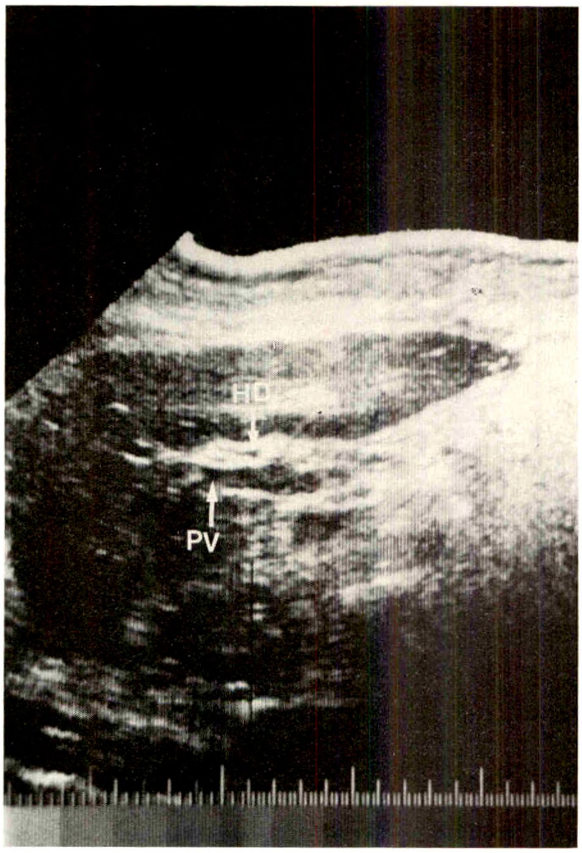

FIG. 1.

A transverse scan showing the main right portal vein (PV) and above it the main right hepatic duct (HD).

TABLE II

NON-OBSTRUCTIVE JAUNDICE

Diagnosis	Patients	Ultrasound diagnostic
Hepatitis	20	4 (all severe changes)
Cirrhosis and fatty infiltration	13	11(84%)
Cardiac cirrhosis	3	3(100%)
Metastases	5	5(100%)
Totals	41	23(56%)

and II. There were no false positives and three false negatives. All the false negatives were in patients with intermittent biliary obstruction due to gallstones. In two cases calculi were demonstrated in the gall-bladder but dilated ducts were not seen. Laparotomy was, however, three weeks later in one instance and five weeks later in the second, when in both cases calculi were found in a dilated common bile duct. The third failure is described in more detail later. The accuracy of separation into two main groups was 97% in this series. When the ultrasound report records the precise cause of jaundice these results are classified as diagnostic. In obstructive jaundice a further category is identified in which the ultrasound report indicated the level of obstruction or contributed other helpful, but non-diagnostic information about the nature of the obstruction. These are classified as helpful.

Diagnostic results were obtained in a total of 52 patients (58%), and helpful results in a further 13%. In the series there were 18 cases of pancreatic carcinomas, 12 of which (66%) were demonstrated. There were 19 patients with stones in the common bile duct which were identified in 11 cases (58%). All the five patients with metastases were correctly identified. In 15 cases of non-obstructive jaundice a bright liver echo pattern was identified. We consider this indicative of cirrhosis, fatty infiltration or severe hepatitis (Dewbury *et al*, 1979). Biopsy in these cases indicated one of these pathologies in all instances. In three patients a bright liver echo pattern was identified in association with enlargement of the IVC and hepatic veins. All these patients were in severe congestive heart failure, one came to post mortem within two weeks and the liver showed the typical changes of cardiac cirrhosis. Two patients with cirrhosis had normal ultrasound images as did the majority of patients with hepatitis.

ILLUSTRATIVE CASE REPORTS

Case 1

A 72-year-old man presented with a three-week history of progressive jaundice. On physical examination, the liver and gall-bladder were enlarged. The bilirubin was 12 mg% and the liver function tests suggested an obstructive aetiology. An ultrasound examination was performed within 48 hours of admission. This confirmed the presence of enlarged ducts within the liver (Fig. 2A and B). The common bile duct was identified measuring 20 mm in diameter and this was traced down to its lower end where it terminates in a large pancreatic mass. Multiple metastases were also demonstrated in the liver. The ultrasound diagnosis was of extrahepatic biliary obstruction secondary to a large pancreatic carcinoma with liver metastases. These findings were all confirmed at laparotomy.

Case 2

A 56-year-old woman presented with a ten-day history of jaundice initially associated with pain. An ultrasound examination was performed. This showed moderate dilatation of intrahepatic biliary radicles and marked enlargement of the common bile duct (Fig. 3). This measured 18 mm in diameter. At the lower end of the common bile duct a 2 cm calculus is demonstrated with distal acoustic shadowing. These findings were confirmed at laparotomy.

Case 3

A 43-year-old man with several months history of vague abdominal discomfort and a five-day history of jaundice was admitted to hospital for further investigation. He was a publican and admitted to a large alcohol intake. Physical examination revealed an enlarged, slightly tender liver. The bilirubin level was 5 mg%. An ultrasound examination demonstrated considerable hepatic enlargement with no evidence of dilated biliary ducts. The liver echo pattern was brightly reflective suggesting fatty infiltration and/or cirrhosis (Fig. 4A and B). A liver biopsy confirmed an established mixed pattern cirrhosis with a minor degree of fatty deposition.

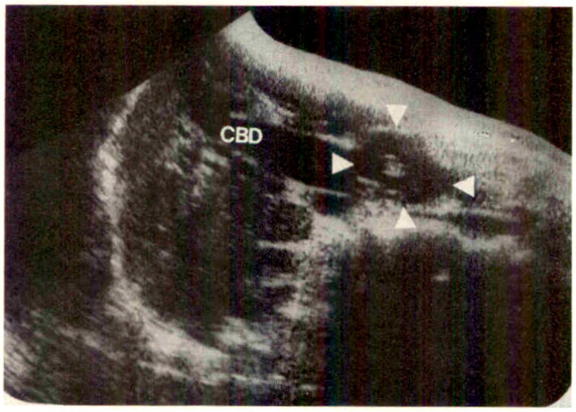

FIG. 2A.

Longitudinal scan showing the full length of the common bile duct (CBD) with an irregular heterogenous mass at its lower ends (arrowheads) typical of a pancreatic tumour.

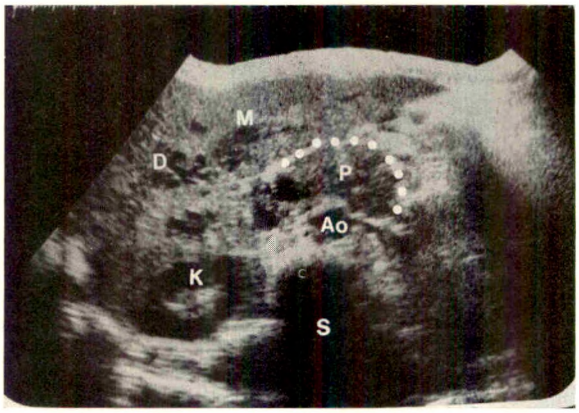

FIG. 2B.

Transverse scan in the same patient showing the full extent of the pancreatic mass (P). Dilated ducts (D) within the liver and metastases (M) are also shown. K=Kidney; S=Spine; Ao=Aorta.

DISCUSSION

The value of ultrasound imaging as a tool for separating obstructive jaundice from other causes of jaundice is confirmed in our series with an accuracy of 97%.

We would like to stress that in over half the patients a further step can be taken in making a definitive diagnosis by ultrasound. This compares favourably with the experience of other workers (Taylor and Rosenfield, 1977). In obstructive jaundice this will obviate the need for further investigatory procedures such as PTC and ERCP prior to laparotomy. The commonest causes of obstructive jaundice are carcinoma of the pancreas and common bile duct stones. We were able to make

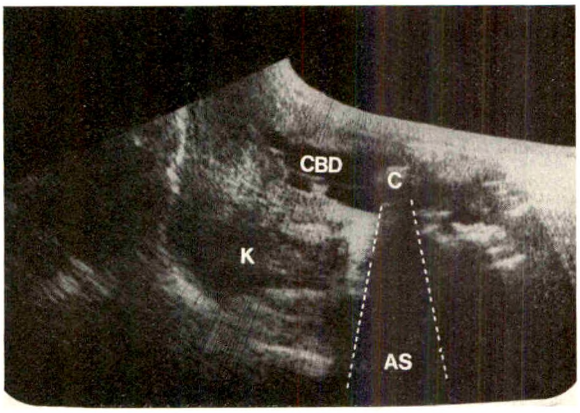

Fig. 3.
Longitudinal scan showing the dilated common bile duct (CBD) with a calculus (C) at its lower end. The acoustic shadowing (AS) is readily visible.

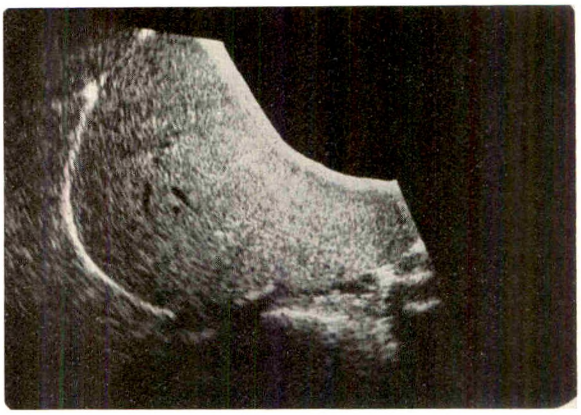

Fig. 4a.
A longitudinal scan through the right lobe of the liver. This shows hepatic enlargement and a brightly reflective echo pattern. Compare appearances with Fig. 4b.

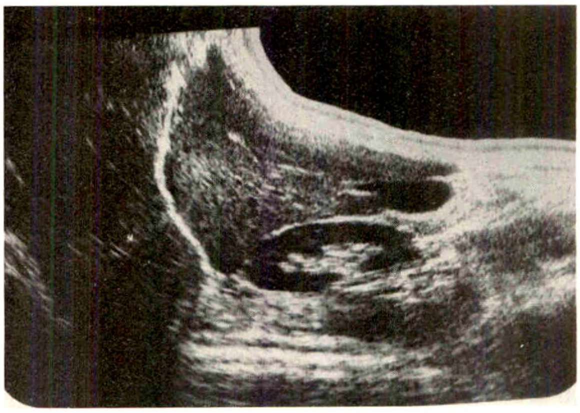

Fig. 4b.
Normal liver for comparison.

positive diagnoses in 66% and 58% respectively of these conditions. Two of the pancreatic carcinomas not visualized were under 3 cm in diameter. The key to the making of a complete diagnosis in obstructive jaundice is the good visualization of the common bile duct. We have noted during this study that our ability to visualize the common bile duct has increased since we have adopted the technique of rotating the patient into the right anterior oblique position to obtain optimal results. For this reason we anticipate that our diagnostic accuracy will increase.

The regular identification of the normal calibre common bile duct is more difficult. It is well recognized that in a small number of patients with obstructive jaundice the common bile duct may not be enlarged. In our series we had one such patient (the third false negative) with a history of several attacks of typical biliary colic over a six-month period, culminating in jaundice in the last attack. Jaundice had been present for over two weeks when the ultrasound examination was done and this did not show any evidence of dilated ducts. The presence of calculi in a non-dilated common bile duct was demonstrated by ERCP and these were later removed at laparotomy. This case emphasizes the point that in the presence of a clinical history of obstructive jaundice with biochemical findings also pointing to an obstructive aetiology, further diagnostic studies may need to be carried out in the presence of a negative ultrasound examination. This can either be a HIDA isotope scan or the more invasive procedures of endoscopic retrograde cannulation of the papilla (ERCP) or percutaneous transhepatic cholangiography (PTC).

In non-obstructive jaundice the ability to make a positive diagnosis rests essentially in the detection of either metastases or the bright liver echo pattern corresponding to cirrhosis, fatty infiltration or severe hepatitis. In this series 23 positive diagnoses were made (56%). Not surprisingly all the patients with metastatic replacement were correctly identified. The overall accuracy achieved will obviously depend on the proportion of such cases in the series. If this group contained mainly cases of moderately severe infective hepatitis the diagnostic possibilities are more limited. Some of the patients with longstanding hepatitis showed a relatively non-reflective echo pattern in the liver. We have begun to recognize this since completion of data for this study. Its significance and its cause are not yet clear. We have shown that the non-reflective halo in the target metastasis is associated with sinusoidal ectasia in post mortem liver studies. Attention to this finding of a relatively non-reflective transonic liver may help in positively identifying the patient with hepatitis. We are at present evaluating this finding more fully.

Conclusion

Ultrasound accurately categorizes jaundice into two main groups and should undoubtedly be the screening method of choice, performed as early as possible in the assessment of the jaundiced patient. In over half the patients a definitive diagnosis may be reached. This is of considerable importance in the management of the patient with obstructive jaundice. In these instances more invasive procedures such as PTC and ERCP need not be performed. Where appropriate, laparotomy may be proceeded to with no further investigatory delay.

REFERENCES

Behan, M. and Kazam, E., 1978. Sonography of the common bile duct: value of the right anterior oblique view. *American Journal of Roentgenology, 130,* 701–709.

Conrad, M. R., Landay, M. J. and James, J. O., 1978. Sonographic "parallel channel" sign of biliary tree enlargement in mild to moderate obstructive jaundice. *American Journal of Roentgenology, 130,* 279–286.

Joseph, A. E. A., Dewbury, K. C. and McGuire, P., 1979. Ultrasound in the detection of chronic liver disease (the "bright liver"). *British Journal of Radiology, 52,* 184–188.

Malini, S. and Sabel, J., 1977. Ultrasonography in obstructive jaundice. *Radiology, 123,* 429–433.

Taylor, K. J. W., Carpenter, D. A. and McCready, V., 1974. Ultrasound and scintigraphy in the differential diagnosis of obstructive jaundice. *Journal of Clinical Ultrasound, 2,* 105–116.

Taylor, K. J. W. and Rosenfield, A. T., 1977. Grey-scale ultrasonography in the differential diagnosis of jaundice. *Archives of Surgery, 112,* 820–825.

Book reviews

Recent Advances In Ultrasound Diagnosis. Edited by Asim Kurjak, pp. iii+330, 1978 (Excerpta Medica, The Netherlands), $52.25.

This book is the Proceedings of the International Symposium on Recent Advances in Ultrasound Diagnosis held in Dubrovnik in October, 1977. The book consists of photo copies of the précis submitted by the authors together with pictures which appear to have reproduced well. The contents vary in quality more than most books with multiple authors, because of the absence of any editorial alteration in the submissions. Some have quaint English and spelling. Despite the variations in type face, it is easily read.

The quality of pictures from the various centres is remarkably wide, varying from the virtually incomprehensible to the superb examples provided by Kossoff and his colleagues in Australia, and one must agree with Donald in his introduction, who points out that "No diagnostic technique can be better than the diagnostic ability of the clinician." There seems no doubt that the important part of an ultrasound examination remains the operator who carries out the procedure and interprets the results.

There are 39 articles in all, of which 16 are on obstetrics and gynaecology. The liver attracted little attention. Poor results are again reported in ultrasound of the breast, which is disappointing considering the superficial nature of the organ, and the wide application this examination would have if it were successful. Striking results are reported in the assessment of blood vessels, from Drs. White and Curry from Ontario, and other workers also report their experience in this field.

The book will be read with interest by workers developing ultrasound techniques. It contains a fair number of up-to-date references, and is recommended for the libraries of ultrasound departments carrying out research.

J. G. B. Russell.

Prevention and detection of cancer. Part I: Prevention Vol. 1: Etiology. Edited by H. E. Nieburgs, pp. xx+1193, illus., 1977 (Marcel Dekker Inc., New York), Sw.Fr.190.

This volume on the aetiology of cancer is the first of four which will present the contributions to the Third International Symposium on Detection and Prevention of Cancer held in New York City from April 26 to May 1, 1976. The preface states that the four volumes aim to "provide a comprehensive review of our current state of knowledge on the role of experimental and human oncogenesis and of host and environmental factors for primary and secondary prevention," constituting a "multidisciplinary approach to cancer control that bridges fundamental research and clinical oncology." With such ambitious aims, it is to be expected that the first volume devoted to the important and basic subject of aetiology should be lengthy and expensive. And, at about 1200 pages and priced at over Sw.Fr.190, it is both of these. It is disappointing, therefore, to find that this work is not comprehensive and includes little that is not available elsewhere.

The chapter on radiation is the shortest in the book with only three contributions. Of these, two report small series of radiation-related malignancies. The third paper by C. E. Land and D. H. McGregor deals with the induction period of radiation-induced malignancy. Whereas radiation-induced leukaemia occurs at an earlier age than the average, no such tendency is shown by the radiation-induced cancers of the lung and breast. The suggestion is made that the increased incidence of lung and breast cancer following radiation exposure depends on the additional operation of factors similar to those that influence the development of these cancers in the general (non-exposed) population.

Most of the book is devoted to laboratory work and not to the epidemiology of cancer in man as the title might suggest to many readers.

L. Kinlen.

1979, *British Journal of Radiology*, *52*, 281–288 APRIL 1979

Grey-scale ultrasonic characteristics of carcinoma of the pancreas

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ABSTRACT

Fifty-five sonograms were performed on 25 cases of surgically and histologically proven carcinoma of the pancreas. The sonographic appearances of the tumour were determined. A diffuse echogenic pattern with irregular margin was the most common appearance. Displacement and indentation of the inferior vena cava and superior mesenteric vessels, greatly assist in localizing the tumour to the pancreas. A reliable prediction of tumour size and resectability cannot be determined by sonography alone. Sonography is helpful in assessing the response of unresectable pancreatic carcinoma to therapy. A more sonolucent appearance of the tumour occurs following chemotherapy.

The recent ultrasound literature contains numerous reports on the normal appearances of the pancreas (Haber *et al.*, 1976; Weill *et al.*, 1977; Doust and Pierce, 1976; Doust, 1975) the vascular anatomy of the upper abdomen as it relates to the pancreas (Sample, 1977; Filly and Carlson, 1976*a*, *b*) and the accuracy of ultrasonic examination in the diagnosis of various pancreatic conditions (Leopold, 1975; Weill *et al.*, 1975). This study was undertaken to determine the grey-scale ultrasonic appearances of carcinoma of the pancreas, the displacement and distortion of the local anatomy, and the relative frequency of these manifestations, in an attempt to define the ultrasonic criteria leading to a diagnosis of carcinoma of the pancreas.

PATIENT MATERIAL

All sonographic abnormalities detected in the pancreatic area between March 1975 and June 1977 were reviewed. A total of 25 cases with surgical and histological proof of pancreatic carcinoma were obtained. These form the basis of this report. There were 19 males and six females with the ages of the patients varying from 41 to 79 years.

METHOD OF EXAMINATION

Ultrasound scans of the abdomen were performed using commercially available grey-scale equipment.† The patients were initially examined in the supine position. Transverse ultrasonic scans were obtained covering the area from the umbilicus to the xiphoid process at 1 cm intervals, and sagittal scans 1 cm apart were performed across the same area. Angled subcostal scans, and prone scans to delineate the area of the tail of the pancreas were performed when necessary. A 2.25 MHz transducer with long internal focus was routinely used, and a 3.5 MHz medium focused transducer was used when the patient's build permitted. The paranchymal detail and vascular anatomy were enhanced by the use of the latter transducer. In some selected cases, a real time scanner (Advanced Diagnostic Research (ADR)) was employed to confirm the presence of indentation of the inferior vena cava.

Anatomical boundaries of the pancreas

Delineation of the pancreas is now possible in the majority of patients (Haber *et al.*, 1976; Weill *et al.*, 1977) despite the variable anatomy of the organ (Kreel *et al.*, 1973). Attention to detail of the adjacent vasculature usually facilitates demonstration of the head and body of the pancreas (Filly and Carlson, 1976*b*; Weill *et al.*, 1975; Skolnick and Royal, 1976). In the transverse scans, the splenic vein and the superior mesenteric vessels, lying anterior to the aorta and vena cava, delineate the posterior aspect of the head, body and tail of the pancreas. One or two centimetres inferior to the level of the splenic vein, the superior mesenteric vein lies to the right of the superior mesenteric artery and is slightly anterior to it. The superior mesenteric vein usually lies anterior to the aorta (Fig. 1A), although it may lie in the mid-line or to the right of mid-line. Recent attention has been drawn to the normal common bile duct, and the gastroduodenal artery together with the duodenal loop and gastric antrum in delineating the anterior and lateral aspects of the pancreatic head (Sample, 1977). The lateral extent of the tail of the pancreas reaches the hilum of the left kidney. In the sagittal scans, the inferior surface of the liver helps delineate the anterior extent of the head and body of the pancreas. The superior extent of the head is marked by the portal vein and the posterior extent of the head by the inferior vena cava. The superior

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†Picker EDC Grey scale—Searle Pho/Sonic—SM.

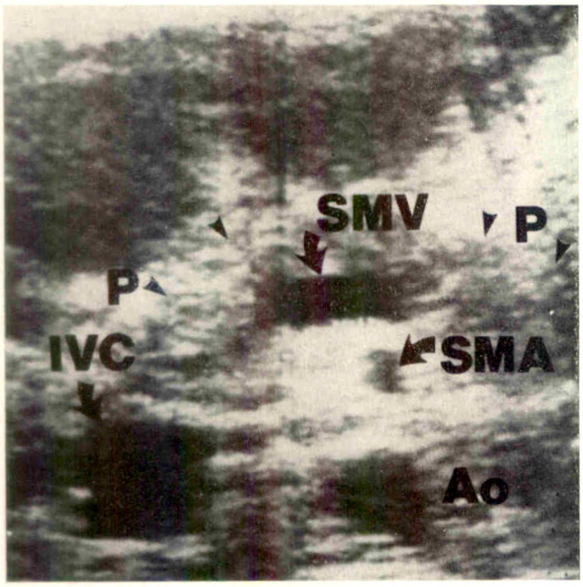

FIG. 1A.

A normal transverse scan at the level of the junction of the superior mesenteric vein (SMV) and splenic vein. (P = pancreas, SMA = superior mesenteric artery, Ao = aorta, IVC = inferior vena cava).

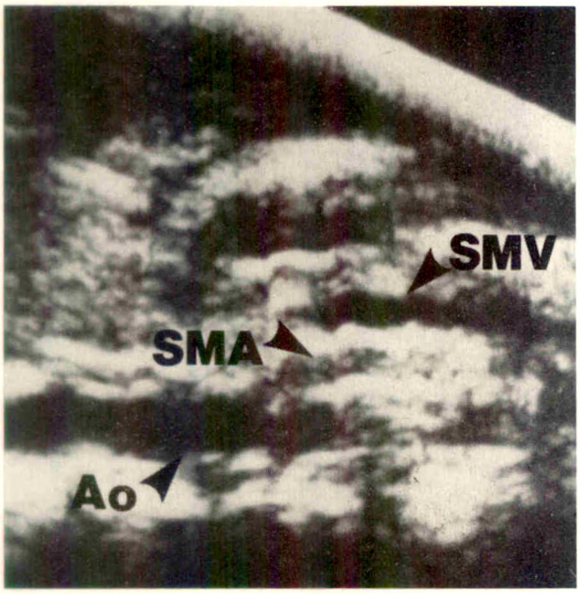

FIG. 1B.

Sagittal scan through the aorta (Ao) showing normal vascular anatomy. The superior mesenteric vein (SMV) lies anterior to the superior mesenteric artery (SMA).

mesenteric vein can be visualized on the sagittal scan anterior to the aorta in the mid-line, and less commonly anterior to the vena cava. The body of the pancreas lies anterior to the superior mesenteric vein and the uncinate process of the head lies posterior to the superior mesenteric vein. The superior mesenteric vein usually follows a parallel course in relation to the great vessels, but may show a slight anterior angulation in relation to the great vessels (Fig. 1B).

Size of the normal pancreas

Various measurements have been supplied for the normal thickness of the pancreatic head, body and tail. The figures given by Haber *et al.* (1976) show a maximum upper limit of normal on transverse scans of 3.4 cm for the head, 2.9 cm for the body, and 2.8 cm for the tail and correspond well with our experience. We regard with suspicion a pancreatic head with a measurement of 3.5 cm or greater, a body of 2.5 cm or greater and a tail of 3.0 cm or greater. It must be re-emphasized that oblique scans are necessary to assess the AP diameter of the organ fully. A greater variation is found in measurements of the cranio-caudad diameter of the pancreas due to its anatomic configuration, and also the fact that the body and tail are not as clearly defined on sagittal scanning.

RESULTS

A total of 55 ultrasonic examinations were performed on the 25 cases of surgically and histologically proven carcinoma of the pancreas. These 55 sonograms were analysed for the location, size and internal echo characteristics of the pancreatic mass. In addition analysis of the vascular anatomy and any associated distortion, as well as secondary signs of pancreatic neoplasm was performed.

Analysis of the characteristics of the pancreatic mass

1. *Location.* In 16 patients the pancreatic mass was localized to the region of the head. The mass in the remaining patients involved the region of the head and body of the five cases, the body in two cases and the tail in two cases.

2. *Size of the mass demonstrated.* The size of the mass demonstrated ranged from 3 cm to 7 cm in diameter, with an average of 5 cm. The actual size of the carcinoma at surgery and autopsy was correlated to the size of the mass measured sonographically. These figures were available in ten cases. Six cases corresponded well to the sonographic size of the lesion. In

the remaining four patients, two of the tumours were smaller and two larger than those measured sonographically. The smallest lesion was a 1 cm carcinoma in an apparent 4 cm tumour mass sonographically.

The level of the mass lesions on the transverse scans varied from 4 cm to 16 cm superior to the umbilicus. The most common level was 6–8 cm above the umbilicus.

3. *Sonographic characteristics of the tumour*. The mass lesion identified in the 25 cases had an irregular margin in each case. No tumour had a completely smooth margin, and there was a wide range of definition of the tumour margin. The echogenic characteristics of the tumour fell into three patterns:

(a) Diffusely echogenic with irregular, internal echoes (52%) (Figs. 2, 3).

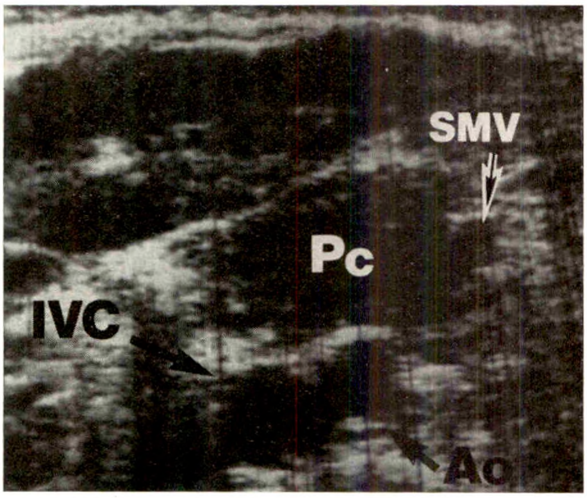

FIG. 2.

Transverse scan—A carcinoma of the body of the pancreas (Pc) demonstrates an irregular echogenic pattern. (IVC= inferior vena cava, Ao=aorta, SMV=superior mesenteric vein).

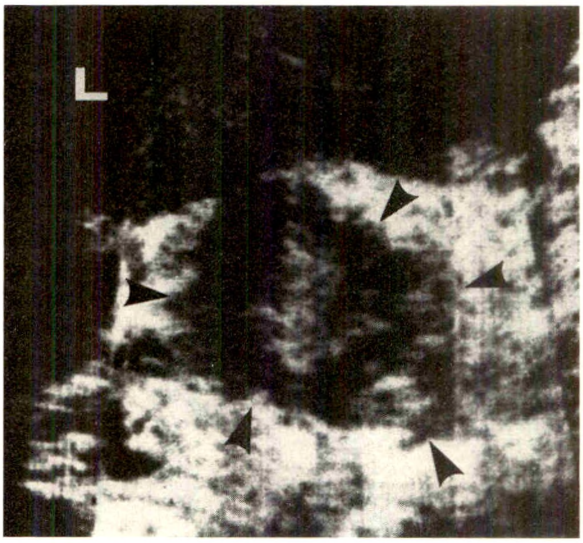

FIG. 4.

Oblique scan of carcinoma of the head of the pancreas demonstrates a tumour mass with a dense central echogenic pattern and sonolucent periphery (arrowheads).

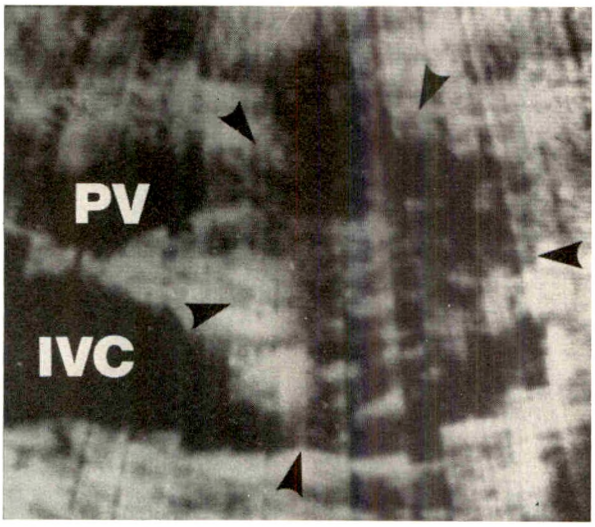

FIG. 3.

Sagittal scan 2 cm to the right of mid-line. Diffuse echogenic carcinoma of the pancreas (arrowheads) is shown markely indenting the inferior vena cava (IVC). (PV=portal vein).

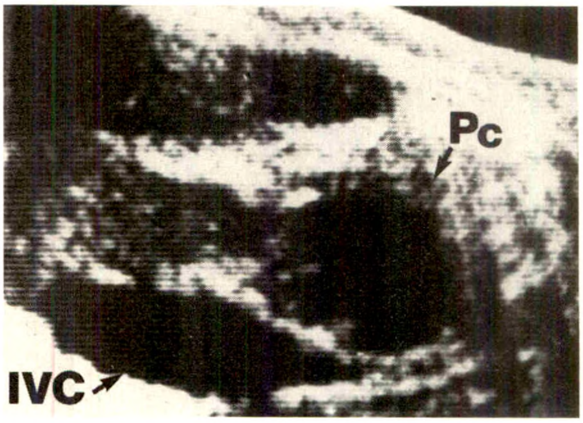

FIG. 5.

Sagittal scan—A sonolucent carcinoma of the head of the pancreas (Pc) is shown markedly indenting inferior vena cava (IVC).

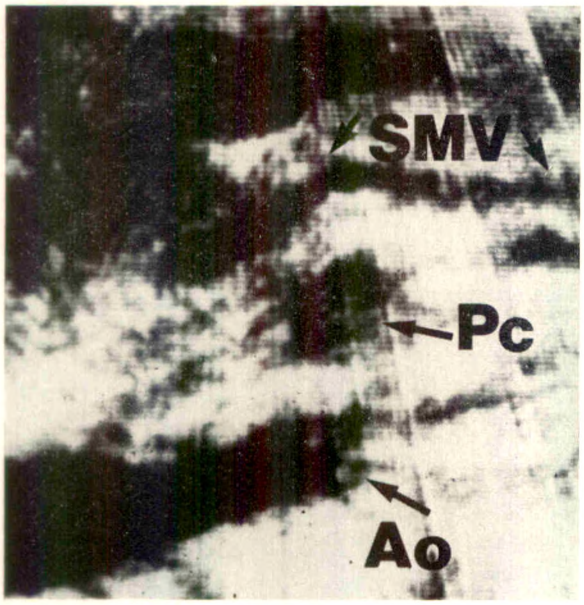

Fig. 6.

Mid-line sagittal scan. Anterior displacement of the superior mesenteric vein (SMV) by carcinoma involving the head and uncinate process of the pancreas (Pc) (Ao = aorta).

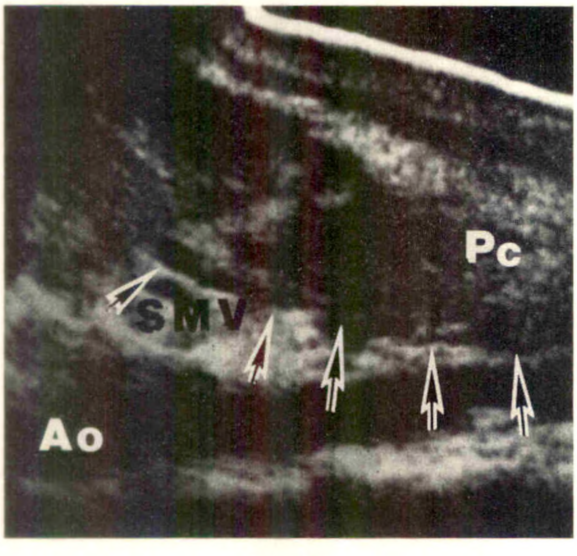

Fig. 7.

Mid-line sagittal scan—Posterior displacement of the superior mesenteric vein (arrows) by a tumour involving the body of the pancreas (Pc) (Ao = aorta).

(b) A central echogenic pattern with a sonolucent periphery (28%) (Fig. 4).

(c) Almost completely transonic with few internal echoes (20%) (Fig. 5).

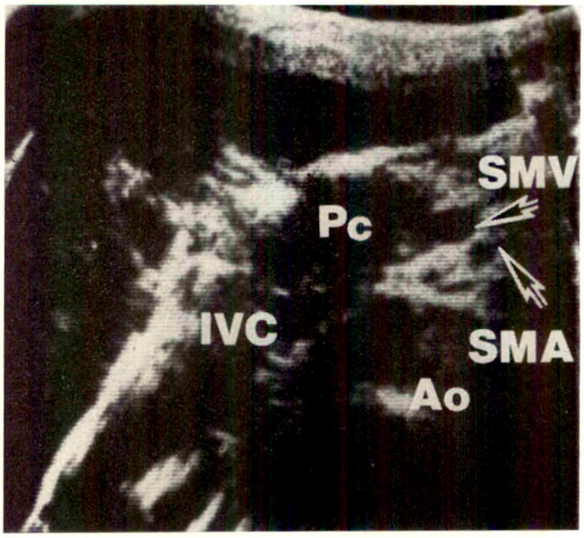

Fig. 8.

Transverse scan—Displacement to the left of the superior mesenteric vein (SMV) and superior mesenteric artery (SMA) by tumour involving the body and head of the pancreas (Pc). (Ao = aorta, IVC = inferior vena cava).

Acoustic attentuation or enhancement by the tumour was not a significant feature in any of these examinations.

Analysis of the vessels

(a) *Inferior vena cava.* Compression of the inferior vena cava was seen in eight of 16 patients with carcinoma localized to the region of the head (Figs. 3, 5), and in two cases with the mass lesion occupying the head and body of the pancreas, a total of ten cases (40%). The presence of constant indentation was confirmed by visualizing the vena cava in all phases of respiration, and with the patient performing the Valsalva manoeuvre. It was also studied by utilization of a real time scanner in some cases.

(b) *Superior mesenteric vessels.* Angulation of the superior mesenteric vein on the sagittal scan in either an anterior (Fig. 6) or posterior (Fig. 7) direction was demonstrated in six cases (24%). The posteriorly displaced SMV should be distinguished from a dilated common bile duct. This was accomplished by (i) noting extension of the vessel beneath the caudal margin of the pancreatic mass. A dilated common bile duct extended downward from above the portal vein but terminated in the pancreatic mass (ii) establishing the connection of the superior mesenteric vein to the portal vein.

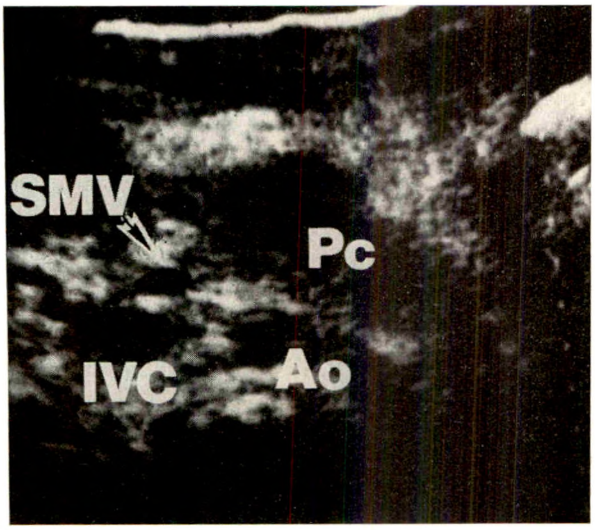

FIG. 9.

Transverse scan—Displacement to the right of the superior mesenteric vein (SMV) by a pancreatic tumour (Pc) involving the body of the pancreas (IVC = inferior vena cava, Ao = aorta).

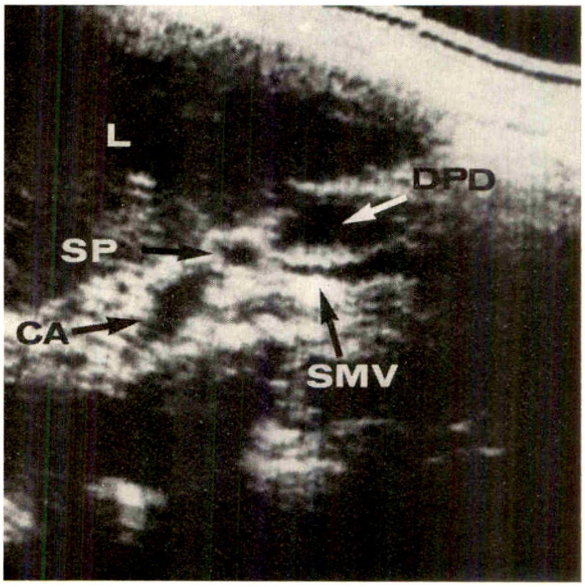

FIG. 10A.

Sagittal mid-line section showing markedly dilated pancreatic duct (DPD). (Sv = splenic vein, SMV = superior mesenteric vein, CA = coeliac axis, L = liver).

Displacement of the superior mesenteric vein and artery may also be observed in the transverse scans. This was noted in seven cases (28%) mainly due to displacement of the superior mesenteric vessels to the left by a mass lesion involving the head (Figs. 2, 8), although displacement to the right may occur (Fig. 9).

(c) *Portal and splenic veins.* In three cases of carcinoma of the head, and in two cases of carcinoma of the head and body there was dilation of the splenic and portal veins. The operative reports in these five patients indicated extensive infiltration of the carcinoma into the adjacent vascular structures.

Analysis of the secondary signs of carcinoma of the pancreas

(a) *Biliary obstruction.* Biliary obstruction as demonstrated by gall-bladder distention and delineation of a dilated common bile duct and/or dilated intrahepatic biliary ducts, was seen in ten patients (48%). In all of these cases the carcinoma involved the head, or the head and body of the pancreas. However, six patients had a by-pass operation prior to attending the oncology clinic, giving a total of 80% of patients who presented initially with obstructive jaundice with a carcinoma involving this area of the pancreas.

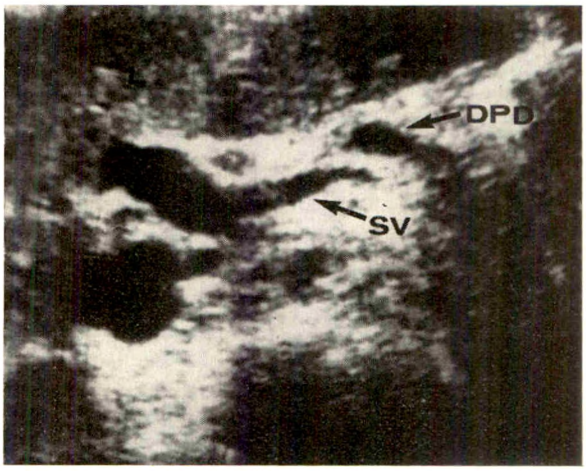

FIG. 10B.

Transverse section showing markedly dilated pancreatic duct (DPD) (SV = splenic vein).

(b) *Liver metastases.* Metastatic deposits in the liver were demonstrated in three cases initially. The carcinoma in these cases involved the head or the head and body of the pancreas. Another six cases developed sonographically demonstrable metastatic involvement during follow-up.

(c) *Ascites.* Moderate to marked degree of ascites was demonstrated in three cases of carcinoma. In two cases the carcinoma involved the head and body and in one case the tail of the pancreas.

(d) *Pancreatic duct dilation.* No definite sonographic evidence of pancreatic duct dilation was demonstrable in this series. However, the majority of cases were performed with the first generation grey-scale equipment. More recent experience with second-generation equipment has enabled us to demonstrate this feature in association with malignancy involving the pancreatic head (Fig. 10A and B).

Progress of the tumour mass

Due to the limited survival time of the patients, most cases had only one or two follow-up sonograms. However, three cases survived for eight months, 18 months, and two years respectively. Analysis of the sonographic characteristics of the tumour on follow-up showed an initially echogenic lesion which became more sonolucent, with a varying degree of central echogenicity. One patient (eight month survival) showed no resolution of the tumour mass and is now deceased. The other two patients, one with a histological diagnosis of a well differentiated adenocarcinoma, and the other with a histological diagnosis of an islet cell carcinoma are still alive and have shown sonographic resolution of the tumour mass, one proven by surgery. Therapy in these cases was a combination of external irradiation, 5-fluorouracil (5 FU) and bischloroethyl nitrosourea (BCNU) in divided doses. A review of the other limited follow-ups indicates that a sonolucent appearance is more common in association with therapy.

DISCUSSION

The vascular anatomy in the region of the pancreatic head is now well accepted as delineating the upper and posterior borders of the pancreas. The lateral margin of the pancreatic head and upper border of the pancreas are also delineated by the gastric antrum and the duodenal loop (Sample, 1977). The duodenal loop separates the pancreatic head from the liver margin and may present a variable appearance depending on whether it is slightly distended with fluid, or whether it contains gas, in which case delineation of the area of the head is very difficult. Confusing echoes may arise from the partially distended duodenal loop in this area. The third part of the duodenum may also be identified posterior to the superior mesenteric vessels where it contributes to the densely echogenic area between these vessels and the aorta and vena cava.

A prominent caudate or quadrate lobe of the liver may cause some confusion with regard to a possible mass in the head of the pancreas. Features which assist in differentiating these from a tumour mass are the demonstration of a similar echo pattern to that of the liver, continuity with the liver and the lack of vascular displacement.

The normal pancreas appears to be characterized by a more echogenic and less discrete echo pattern than the hepatic parenchyma (Haber *et al.*, 1976). This feature does not vary significantly with age, although it is better demonstrated in the younger-more asthenic patient. It serves to identify the pancreas from the more dense echogenic surrounding structures such as the gastric antrum, the duodenal loop, the third part of the duodenum and the perivascular connective tissue.

Two normal intrahepatic structures may be mistaken for metastases: (1) The ligamentum teres may be visualized on transverse scans as a well defined densely echogenic area between the left and right lobes of the liver (Fig. 11A). This cannot be demonstrated on sagittal scans; its position and well defined appearance serve in distinguishing it from a metastatic lesion in the liver. (2) A further dense echo may also be seen in this area due to the perivascular connective tissue surrounding the left branch of the portal vein (Fig. 11B). This can be distinguished from metastatic involvement by demonstrating its relationship to the branches of the portal vein.

Indentation of the inferior vena cava (Walls and Templeton, 1977), was the most common vascular distortion noted in this series. In addition, anterior displacement of the superior mesenteric vein may indicate a mass involving the head and uncinate process, and posterior displacement of the superior mesenteric vein may indicate a mass involving the head and body. Crowding of the superior mesenteric vessels, as well as distortion of the normal relationship between the superior mesenteric artery and the superior mesenteric vein may help in confirming the presence of a mass in the pancreas.

No attempt was made in this retrospective study to calculate the accuracy of ultrasonic diagnosis of pancreatic carcinoma. A review of the material involved does indicate a high degree of accuracy in identifying a mass lesion when the pancreas was adequately visualized.

Pancreatitis localized to one area of the organ still remains difficult to differentiate from carcinoma, especially in view of the fact that the two entities may coexist (Doust *et al.*, 1975; Leopold, 1975). The cases with chronic pancreatitis presenting as a localized mass lesion tend to show a more sonolucent appearance and a coarser echogenic pattern than that encountered with pancreatic carcinoma (Fig. 12). In addition, dense echogenic areas may be present, indicating areas of fat necrosis and calcification, both in the mass and remainder of the gland. However, the appearance of a dense central echo pattern is highly suspicious of an underlying carcinoma, the surrounding sonolucency presumably being due to associated oedema and inflammatory change. The duodenal loop may occasionally simulate this appearance, but is found to be an inconstant feature on repeat scanning. Correlation of the findings with those of clinical and laboratory investigations, as well as arteriography and endoscopic pancreatography enable diagnostic differentiation in these cases.

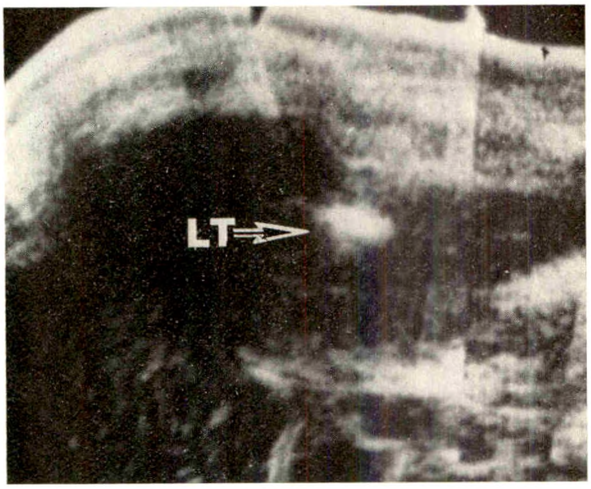

FIG. 11A.

Normal transverse sonogram of the liver shows a dense echogenic area in the left lobe due to the ligamentum teres (LT).

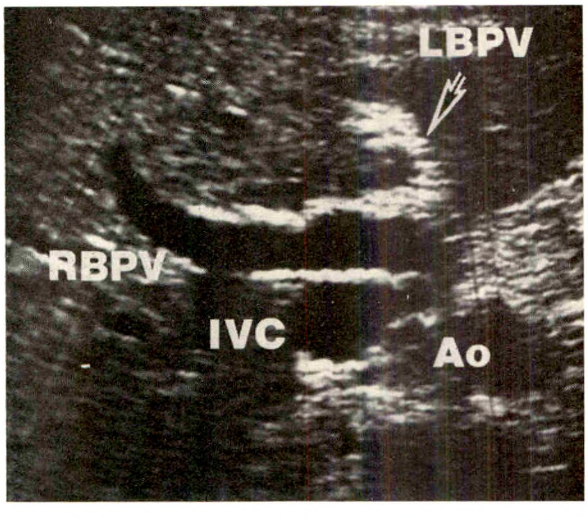

FIG. 11B.

Transverse scan of the liver at the level of the portal vein. A dense echogenic area due to the perivascular connective tissues surrounding the left branch of the portal vein (LBPV) is seen. (RBPV = right branch of the portal vein, Ao = aorta, IVC = inferior vena cava).

The association of a pseudo cyst with a mass lesion within the pancreas is indicative of pancreatitis. However, in rare cases it may also be associated with an underlying carcinoma and associated pancreatitis.

The carcinoma at surgery and autopsy may prove smaller than that indicated sonographically. This feature is not particularly surprising in view of the normal dimensions of the gland. A tumour of 2 to 3 cm size can be expected to displace the adjacent parenchyma as well as invade it and present as an apparent 4 to 5 cm mass lesion. In addition, autopsy findings on those cases where a discrepancy in size was present demonstrated associated pancreatitis contributing to the overall size of the mass evaluated sonographically. The greatest discrepancy was in a 1 cm tumour which presented as an apparent 4 cm mass. These observations indicate that sonography cannot be expected to give a realiable prediction as to resectability and arteriography and ERCP are indicated where resection of the tumour is considered (Ariyama *et al.*, 1977).

However, it is debatable if resection of the tumour alone increases patient survival. There is increasing

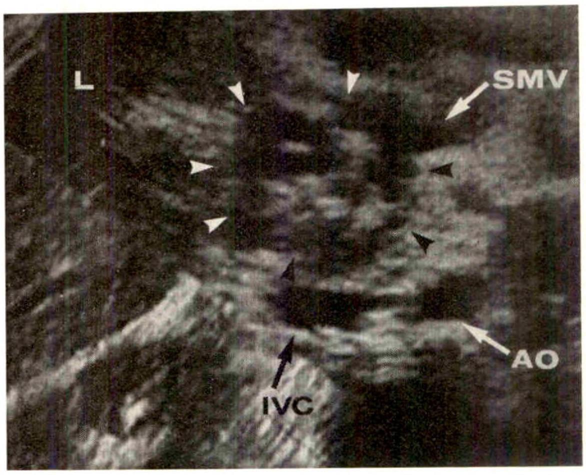

FIG. 12.

Pancreatitis involving head of pancreas (closed arrows). (L = liver, SMV = superior mesenteric vein, IVC = inferior vena cava, Ao = aorta).

evidence that aggressive chemotherapy and radiotherapy increases the survival rate in cases of pancreatic carcinoma following palliative surgery (Lemmon *et al.*, 1973).

The high accuracy of ultrasound in assessing the pancreatic area makes this the initial screening modality of choice, although the full impact of CT scanning, where available, has yet to be determined. The features which aid in establishing the diagnosis of pancreatic carcinoma are (a) the presence of a homogenous mass in the pancreas with an irregular margin and either a diffuse uniform echo pattern, or a more sonolucent appearance with a tendency to central echo clustering and (b) displacement of the adjacent vasculature. In more advanced cases the secondary signs such as obstruction of the biliary tract, metastasis to the liver and ascites aid in establishing the diagnosis. On follow-up examination where it has not been possible to remove the pancreatic carcinoma, a more sonolucent appearance of the tumour may be expected in relation to surgical intervention and therapy.

ACKNOWLEDGMENTS

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REFERENCES

ARIYAMA, J., SHIRAKABE, H., IKENABE, H., KUROSAWA, A. and OWMAN, T., 1977. The diagnosis of the small resectable pancreatic carcinoma. *Clinical Radiology, 28*, 437–444.

DOUST, B. and PIERCE, J. D., 1976. Grey-scale properties of normal and inflamed pancreas. *Radiology, 120*, 654–657.

DOUST, B., 1975. Ultrasonic examination of the pancreas. *Radiological Clinics of North America, 13*, 467–478.

DOUST, B., MAKLAD, N. F. and BAUM, J. K., 1975. Ultrasonic evaluation of pancreatitis. Ed. D. White, in *Ultrasound in Medicine: Proceedings of the 19th Annual Meeting of the American Institute of Ultrasound in Medicine, 1*, p. 194 (Plenum Press, New York).

FILLY, R. A. and CARLSON, E. N., 1976a. Newer ultrasonic anatomy in the upper abdomen. I. The portal and hepatic venous anatomy. *Journal of Clinical Ultrasound, 4*, 85–90.

1976b. Newer ultrasonic anatomy in the upper abdomen. II. The major systemic veins and arteries with a special note on localization of the pancreas. *Journal of Clinical Ultrasound, 4*, 91–96.

HABER, K., FREIMANIS, A. K. and ASHER, W. M., 1976. Demonstration and dimensional analysis of the normal pancreas. *American Journal of Roentgenology, 126*, 624–628.

KREEL, L., SANDIN, B. and SLAVIN, G., 1973. Pancreatic morphology. A combined radiological and pathological study. *Clinical Radiology, 24*, 154–161.

LEMMON, H. M., FOLEY, J. F., PAUSTIAN, F. F., KESSINGER, A., DELEVAN, J. and MCLAUGHLIN, C. W., 1973. Improved palliation of pancreatic carcinoma. *Cancer, 31*, 17–25.

LEOPOLD, G., 1975. Echographic study of the pancreas. *Journal of the American Medical Association, 232*, 287–289.

SAMPLE, W. F., 1977. Technique for improved delineation of normal anatomy of the upper abdomen and high retroperitoneum with grey-scale ultrasound. *Radiology, 124*, 197–202.

SKOLNICK, M. C. and ROYAL, D. R., 1976. Normal upper abdominal vasculature. A study correlating B-scanning with arteriography and gross anatomy. *Journal of Clinical Ultrasound, 4*, 399–402.

WALLS, W. J., GONZALEZ, G., MARTIN, N. L. and TEMPLETON, A. W., 1975. B-scan evaluation of the pancreas. Advantages and accuracy as compared to other diagnostic techniques. *Radiology, 114*, 127–134.

WALLS, W. J. and TEMPLETON, A. W., 1977. Ultrasonic demonstration of inferior vena caval compression. *Radiology, 123*, 165–167.

WEILL, F., EISENSCHER, A., AUCANT, D., BOURGION, A. and GALLINET, D., 1975. Ultrasonic study of venous patterns in the right hypochondrium: an anatomical approach to the differential diagnosis of obstructive jaundice. *Journal of Clinical Ultrasound, 3*, 23–29.

WEILL, F., SCHRAUB, A., EISENSCHER, A. and BOURGION, A., 1977. Ultrasonography of normal pancreas, success rate and criteria for normality. *Radiology, 123*, 417–423.

Book review

Radiologic Examination of the Orohypopharynx and Esophagus. By C. Zaino and T. C. Beneventano. pp. xiii+317, 450 illus. 1977, (Springer-Verlag, Berlin), DM120.00/$60.00.

This is a superb book, its 300-odd pages containing everything that it is necessary to know about the oesophagus. The chapters are short, the printing and illustrations are as one expects from Springer-Verlag—excellent. The authors have managed to combine the anatomy, physiology, pathology and radiology of the eosophagus in a fashion which should ensure a wide readership for this book.

J. A. GLEESON.

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Radionuclide venography in the management of proximal venous occlusion. A comparison with X-ray contrast venography

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ABSTRACT

Ascending contrast venography often fails to show the proximal venous system when there is co-existing occlusion of femoral or iliac veins. Retrograde and pertrochanteric venography both have severe limitations in terms of invasiveness and reliability. Radionuclide venography (RNV) is suggested as a less invasive alternative. 100 patients were investigated by both RNV and X-ray contrast venography (XRV). There was a 72% overall correlation between the two methods of investigation. The proximal definition of XRV was limited in those cases with femoral obstruction. RNV, however gave progressively better views as imaging became more proximal and this was accentuated in the presence of femoral or iliac occlusion. RNV is simple and easy to perform and less invasive than XRV. The definition at calf level is such that it cannot at this stage replace XRV as the standard diagnostic procedure. However, in patients with proximal occlusions it gives more reliable information than that obtainable by ascending contrast venography.

Nine years after its introduction (Webber *et al.*, 1969) radionuclide venography (RNV) is still at the stage of assessment. Its precise role in the diagnosis of thromboembolic disease has yet to be established. This study was undertaken to answer two questions: does RNV provide a simple method of assessment of the proximal deep vein system, especially when femoral or iliac occlusion is present, and is RNV a workable alternative to X-ray contrast venography (XRV) for general diagnostic use?

PATIENTS AND METHODS

The patients studied were referred for venography and isotope lung scanning and comprised the following groups.

Group I. Patients with acute symptoms or signs suggestive of thromboembolism or a positive fibrinogen uptake test (FUT).

Group II. Patients undergoing reassessment after one week's heparin treatment for deep vein thrombosis (DVT).

Group III. Patients undergoing reassessment after three months treatment for deep vein thrombosis.

Group IV. Patients without DVT undergoing venographic evaluation prior to varicose vein surgery.

Group V. Patients referred specifically for evaluation of the proximal deep venous system before, during and after thrombolytic therapy.

Radionuclide venography (RNV)

The patients were examined supine on a mobile horizontal imaging table. Two specially designed 2.5 cm diameter pneumatic cuffs (Millard-London) were applied to each leg, one just above the ankle and the other just above the knee, and connected to a bellows and pressure gauge. A ^{60}Co spot marker was placed in the midline between the legs at the level of the upper border of the patella, another just below the symphysis pubis and a third at the umbilicus. Imaging was carried out using a γ-camera fitted with a diverging collimator. It was found helpful to have a persistence oscilloscope linked to the camera to provide a continuous visual display of the progress of the radionuclide. The pneumatic cuffs were inflated to 100–150 mm Hg and a 21 or 23 gauge butterfly needle inserted into a dorsal foot vein on each side. A three-way stop-cock was connected to permit injection of radionuclide followed by a saline flush. The system was tested with saline at the beginning of each examination. The patient was then positioned for imaging of the calves, with the ^{60}Co marker between the patellae at the top of the field of view.

One mCi of ^{99}Tc^{m}-macro-aggregated albumin (MAA) was injected into each foot, followed by approximately 20 ml saline flush. Imaging commenced and the passage of the radionuclide into the deep veins of the calf was followed on the persistence oscilloscope and recorded on Polaroid film. If necessary each calf was gently compressed once to fill the popliteal vein. If poor calf filling was observed, additional saline was injected. Imaging was complete when 50,000 counts had been accumulated (approximately 30 seconds, intensity 570 units). With the cuffs still inflated, the table was moved to position the patient's thighs in the field of the camera so that both ^{60}Co spot markers were in view at opposite ends of the field. Images were obtained of the femoral veins after a further injection into each foot of 1 mCi MAA, and 30,000 counts accumulated (approximately 60 seconds, intensity 600 units). Finally the patient was positioned with the camera over the pelvis and lower abdomen. The cuffs were released and with a further 10 ml of saline flush and active ankle exercising, images of the iliac veins and inferior vena cava were obtained, accumulating 30,000 counts (approximately three minutes, intensity 600 units). Exercise continued until 30 dorsiflexions of the ankles had been performed. At this stage a persistence film of the calf region was obtained (exposure exactly one minute, intensity 600 units) followed by similar films of the thighs and pelvis at the same setting.

The time taken for RNV was 15 minutes with an additional 15 minutes if a lung scan was required also. Results were available immediately on Polaroid film.

X-ray contrast venography (*XRV*)

The technique of venography used has already been described elsewhere (Kakkar, 1972). Patients were examined on a horizontal table. Tourniquets 2.5 cm wide connected to a pressure gauge and bellows (Millard, London) were placed just above each ankle and knee. The pressure in the ankle tourniquet was adjusted to 100 mm Hg and that in the proximal one to 150 to 250 mm Hg depending on the diameter of the thigh. A 21 or 23 gauge butterfly needle was inserted into a dorsal foot vein each side, secured with adhesive tape, and a trial injection of 5 ml heparinized saline (10 iu/ml) made. A vein on the dorsum of the first toe was selected where possible, although any vein on the dorsum of the foot will suffice and in rare cases use is made of the long saphenous vein just anterior to the medial malleolus. Under X-ray screening control, 25 ml of pre-warmed 60% meglumine iothalamate (Conray 280) was injected slowly. Three standard calf pictures were obtained in anteroposterior, internally rotated and externally rotated positions. The calf was then gently compressed once to fill the popliteal vein and films obtained of this region. A further 10 ml of contrast was injected and the femoral vein filled by gentle calf pressure and a film exposed. Finally, a further 15 ml of contrast was injected. The proximal tourniquet was released and calf pressure applied to fill the iliac veins and inferior vena cava. Immediately after the final film any residual contrast medium was flushed out of the deep veins by the injection of 100 ml of heparinized saline (10 units/ml) and active leg movements.

RESULTS

An immediate assessment of each test was made and recorded in the patient's case folder. Subsequently all films were reviewed in the absence of clinical details.

A positive XRV was defined as a filling defect, present on at least two films, or an area of non-filling with collateral circulation.

A positive RNV was defined as an area of decreased radioactivity (filling defect) with or without collateral circulation; stasis of radioactivity below an obstruction or persistence of radioactivity after exercise (Fig. 1).

A total of 104 patients (208 limbs) were examined. Four patients were excluded from analysis—two because XRV was omitted and two because RNV had to be abandoned for technical reasons. All the remaining 100 had both XRV and RNV performed on the same day. One third had RNV prior to XRV and two thirds had XRV first.

Correlation

The results are shown in Table I. There was an overall correlation between RNV and XRV of 71.5% with 16% false positive and 12.5% false negative results from RNV.

In the calf, there was a correlation of 69% with 16% false positive and 15% false negative results.

In the thigh, there was a correlation of 96% with 1% false positive and 3% false negative results.

In the pelvis, there was 100% correlation—although XRV was often unsatisfactory above the external iliac veins.

Group I—the acute situation (Table II)

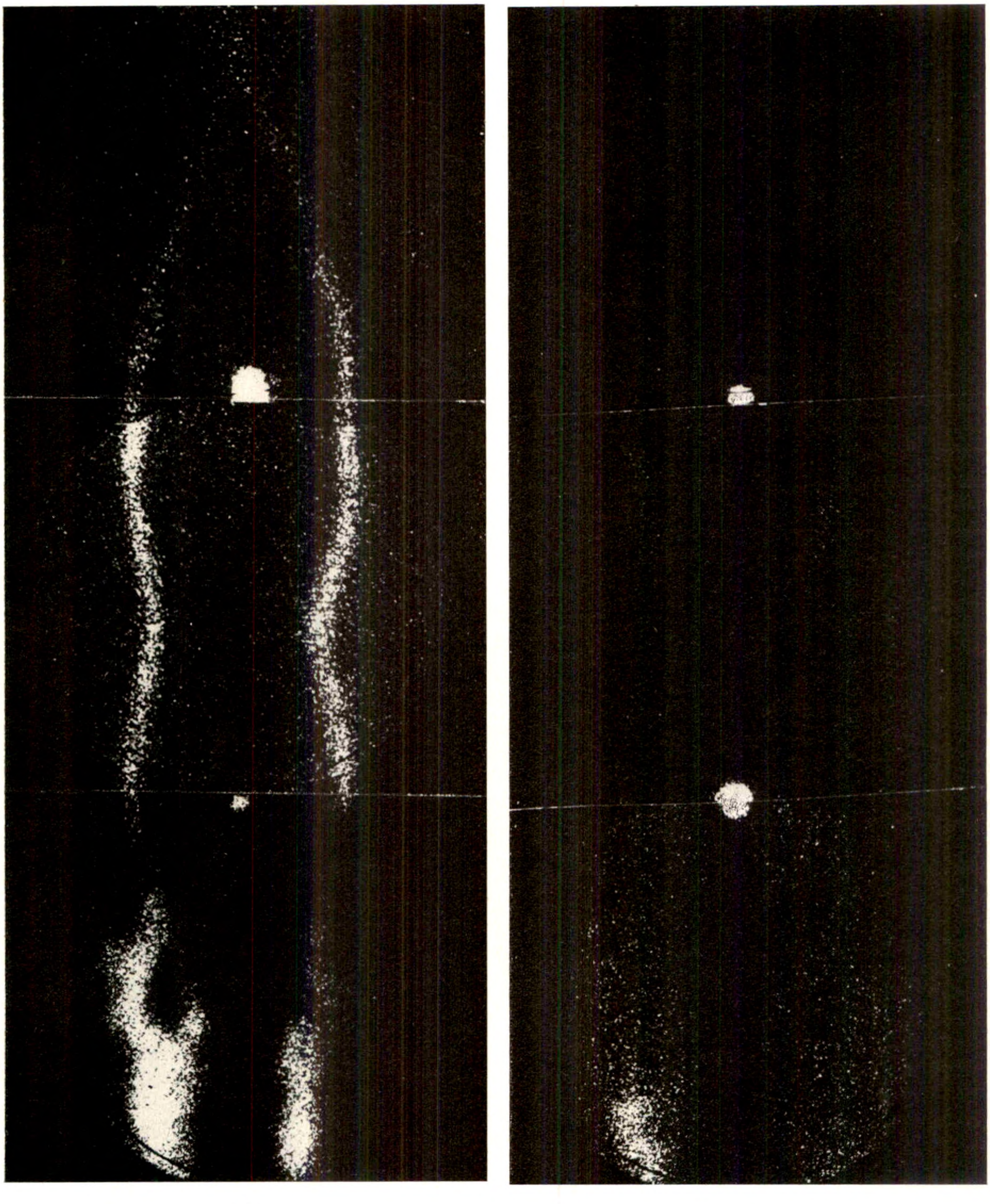
In the acute situation RNV detected 28 out of 38 DVT's (73.7%) with 8.6% false negative and 19.8%

TABLE I
THE CORRELATION BETWEEN RNV AND XRV

		XRV							
		Overall		Calf		Thigh		Pelvis	
		+	−	+	−	+	−	+	−
RNV	+	68	32	59	32	18	2	17	0
	−	25	75	30	79	6	174	0	183

TABLE II
THE RELATIONSHIP BETWEEN RNV RESULTS AND AGE OF THROMBUS

DVT	Detection (%)	Persistence (%)
Acute	73.7	50.5
1 week	86.7	57.1
3 months	39.1	17.4



A B

FIG. 1.

Radionuclide venogram. (A)Dynamic phase. There is a filling defect within the right calf. The remainder of the right side and whole of the left side is normal. (B) Static phase. There is persistence of radionuclide in the right calf distal to the filling defect.

false positive results. Persistence of radionuclide after exercise (hot spot) was seen in 19 out of 38 (50%) of those with thrombi.

Fibrinogen uptake test (*FUT*) (Table III)

Thirteen limbs in which the FUT had become positive postoperatively were examined. Thrombus was demonstrated in the deep veins in nine, of which five had positive RNV. In the remaining four limbs with negative XRV, RNV was positive in three due to persistence of radionuclide in superficial veins.

TABLE III

POSITIVE FIBRINOGEN UPTAKE TEST (FUT)—CORRELATION BETWEEN RNV AND XRV

	XRV	
	Thrombus present	Thrombus absent
	9	4
RNV positive	5	3
RNV negative	4	1

Extent of thrombus (Table IV)

RNV detected seven out of 13 (53.8%) minor thrombi in the calf (defined as those present in soleal veins alone, or in tibial veins but less than 5 cm in overall length). Persistence occurred in five (38.5%).

TABLE IV

THE RELATIONSHIP BETWEEN RNV RESULT AND EXTENT OF THROMBUS

DVT	Detection (%)	Persistence (%)
Minor calf	53.8	38.5
Major calf	80	60.0
Femoral	92.0	50.0
Iliac	100.0	—

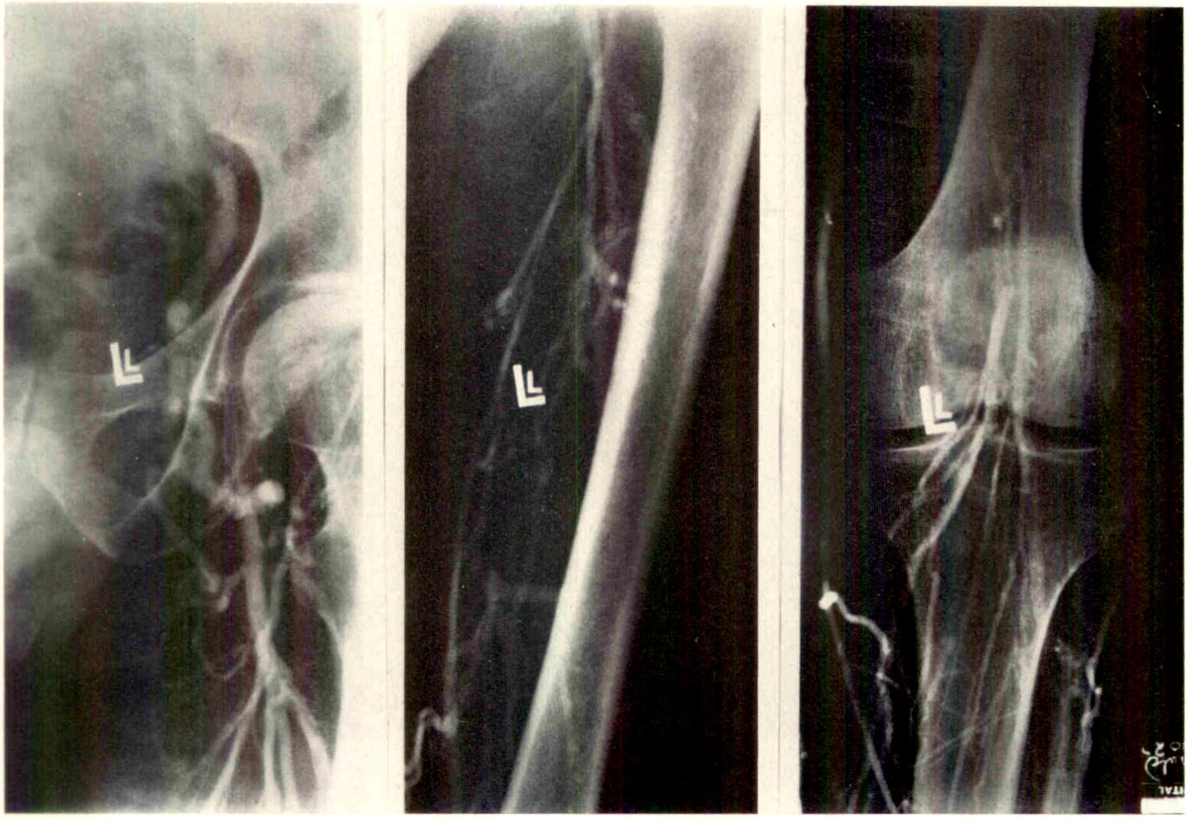
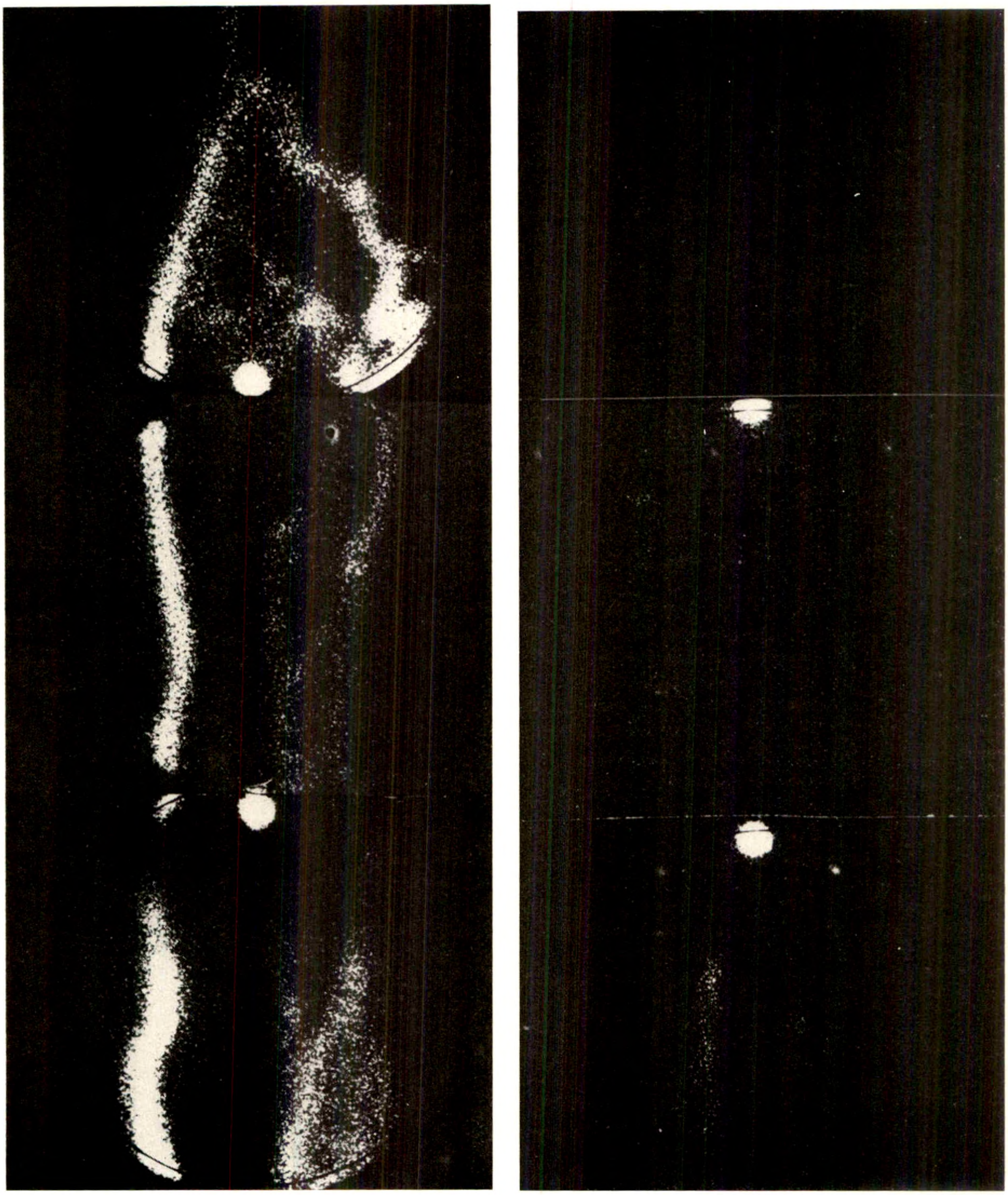


FIG. 2.

X-Ray contrast venogram. There is occlusion of the femoral vein which is replaced by collaterals. There is no filling of the more proximal deep venous system.



A

B

FIG. 3.

Radionuclide venogram (same patient as Fig. 2). (A) Dynamic phase. The whole deep venous system on the left is replaced by collaterals. The right side appears normal. (B) Static phase. A little radionuclide persists in superficial veins of the right calf only.

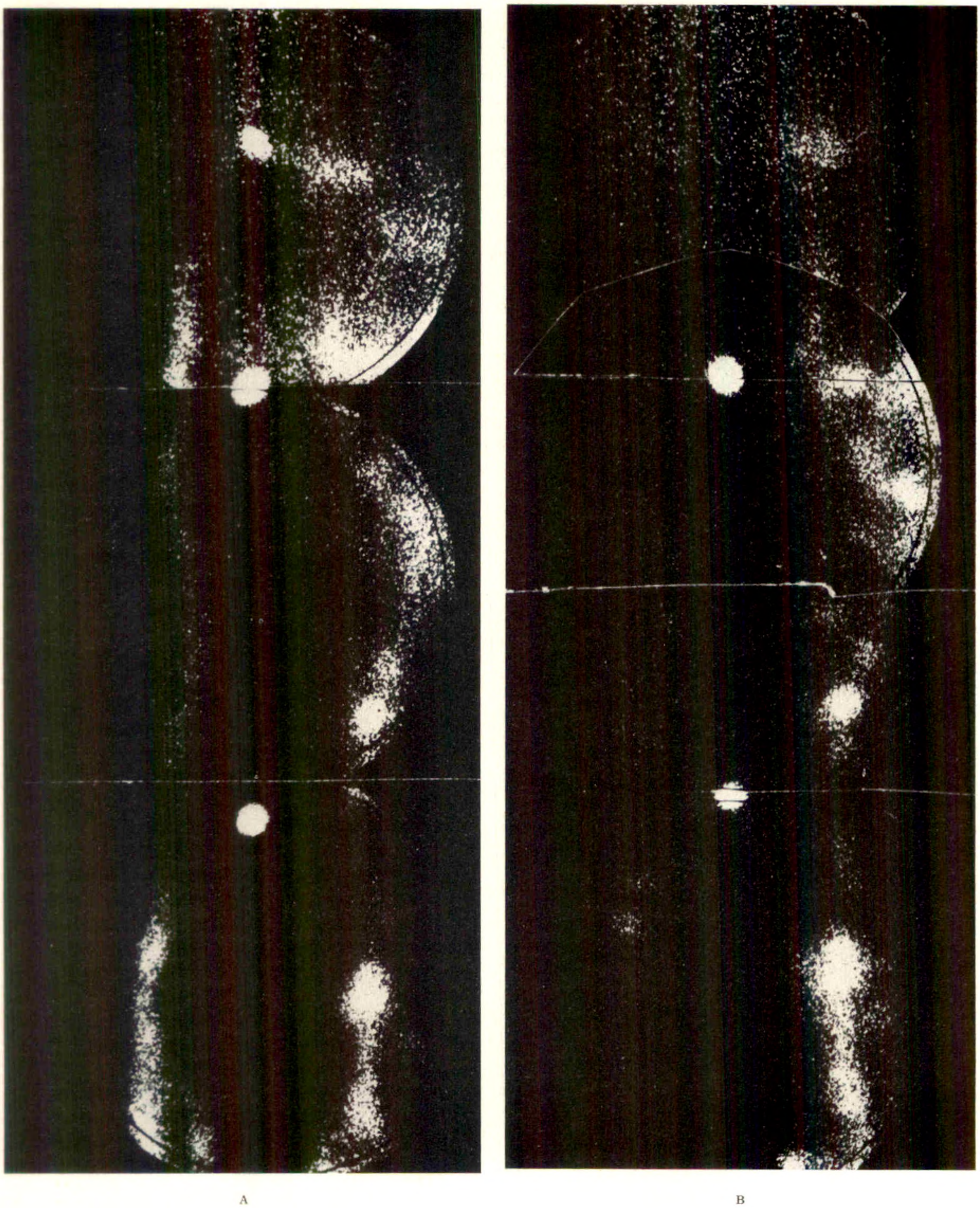
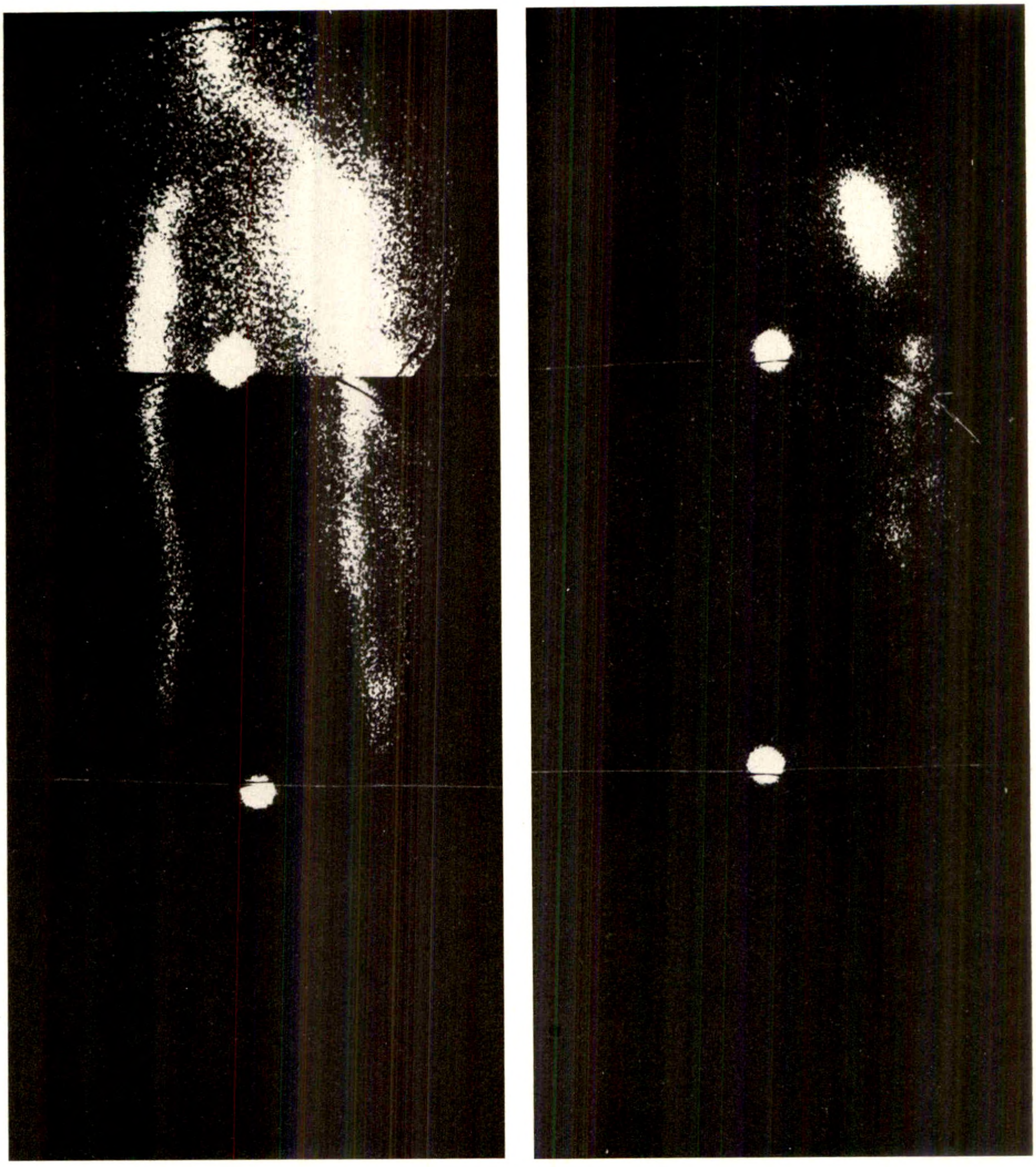


FIG. 4.

Radionuclide venogram before thrombolytic therapy. (A) Dynamic phase. The deep venous system on the left side is totally occluded up to the inferior vena cava with pooling of isotope in collateral circulation. The right side appears normal. (B) Static phase. Radionuclide has cleared from the normal right side, but there is persistence on the left up to the level of the common iliac vein.



A B

Fig. 5.

Radionuclide venogram after three days thrombolytic therapy. (A) Dynamic phase. The left femoral vein is now partially open; radionuclide is trapped distal to the common iliac vein and reaches the inferior vena cava via a collateral. (B) Static phase. Radionuclide persists on the left in the upper femoral and external iliac veins.

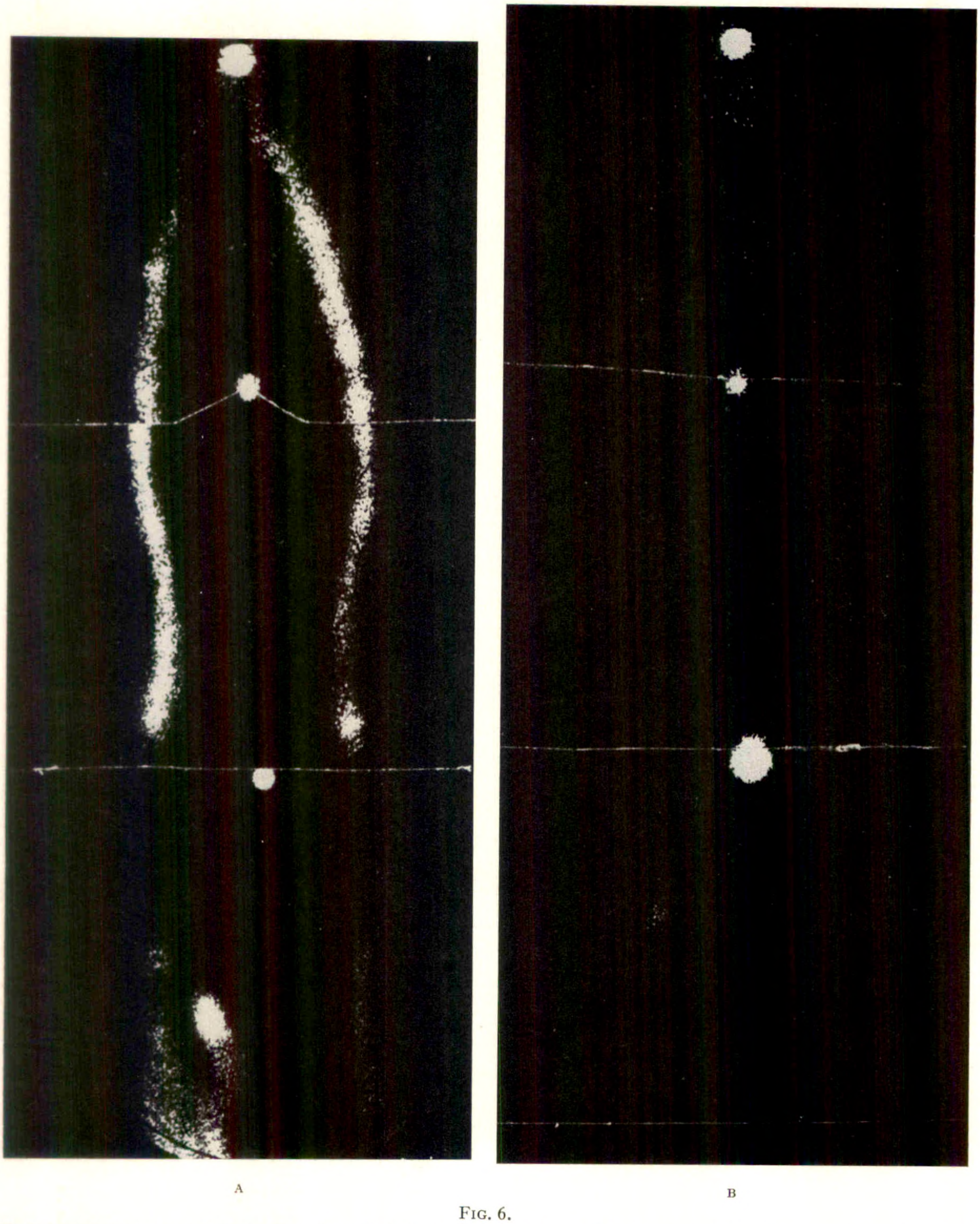


Fig. 6.

Radionuclide venogram after five days thrombolytic therapy. (A) Dynamic phase. The major veins now appear normal indicating lysis of all thrombus. (B) Static phase. There is now no abnormal persistence of radionuclide.

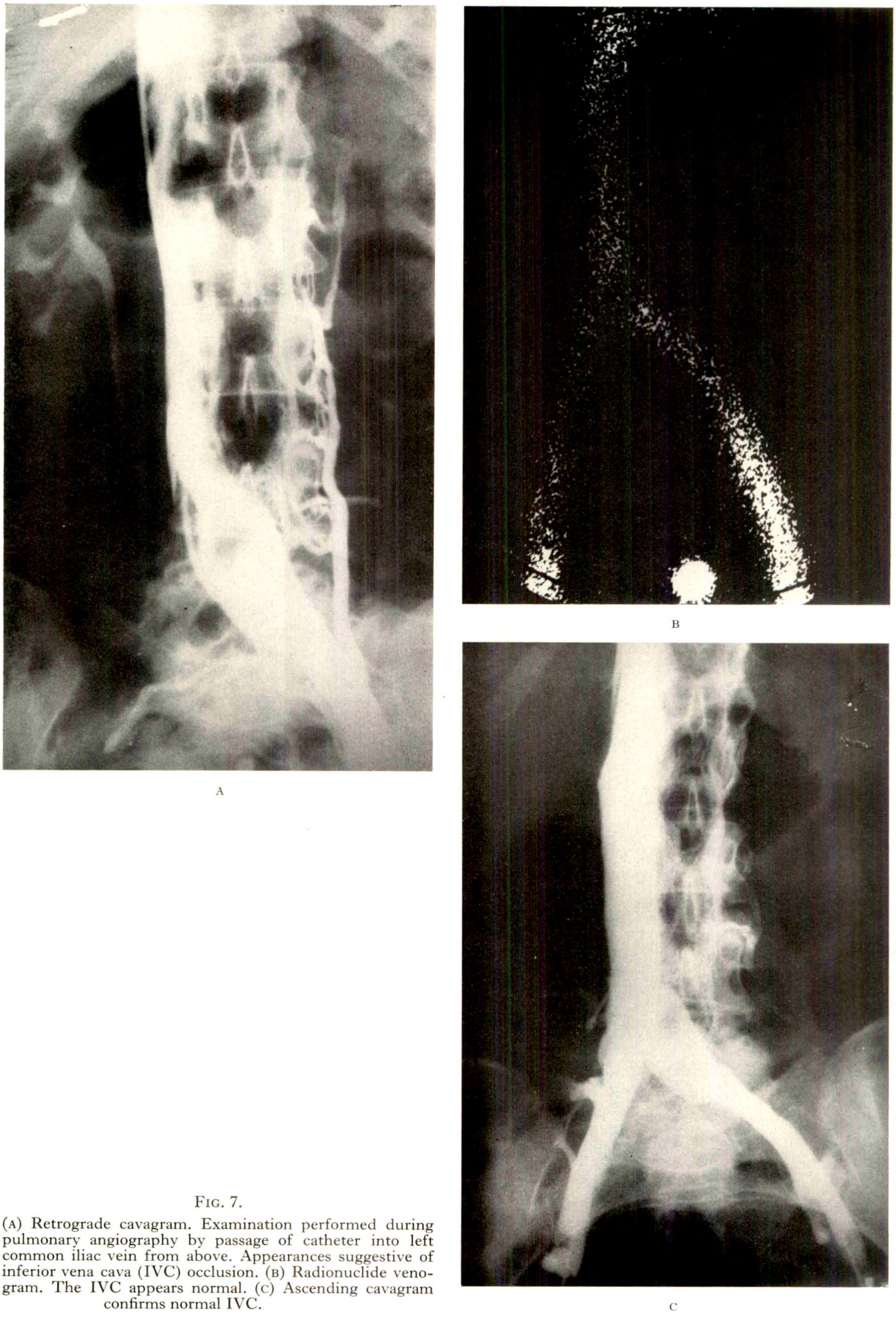
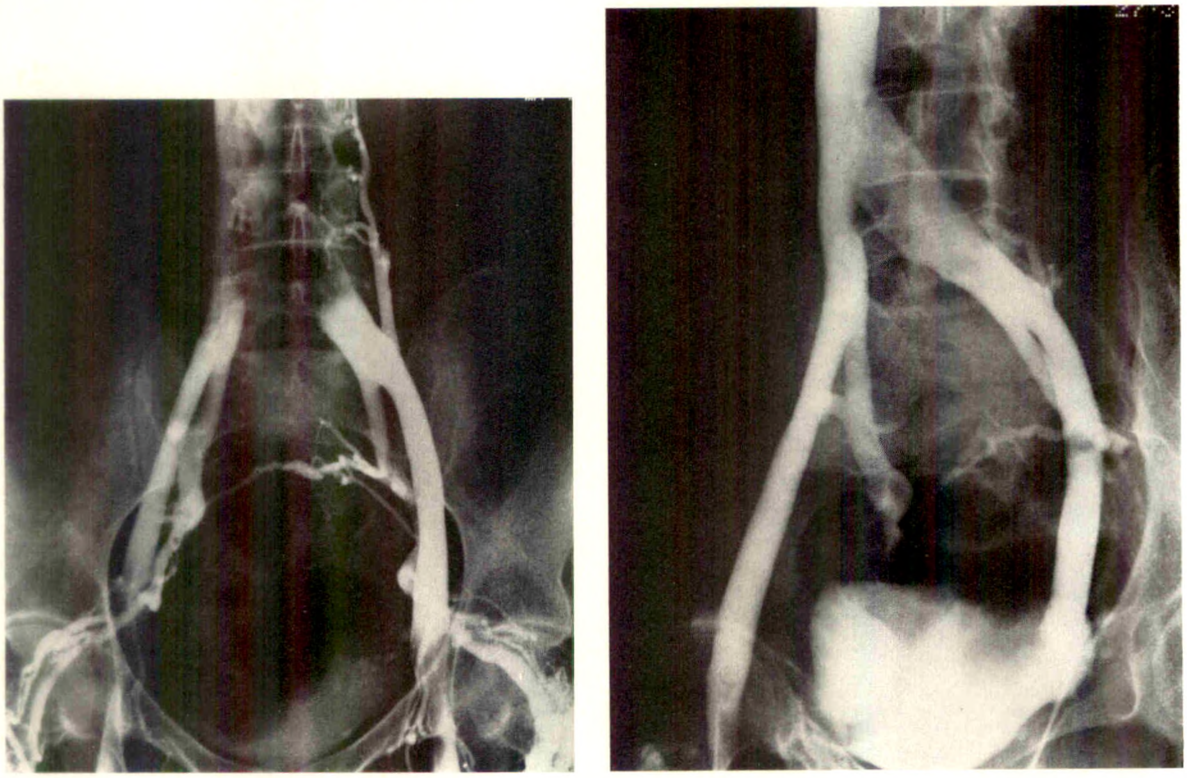


FIG. 7.

(A) Retrograde cavagram. Examination performed during pulmonary angiography by passage of catheter into left common iliac vein from above. Appearances suggestive of inferior vena cava (IVC) occlusion. (B) Radionuclide venogram. The IVC appears normal. (C) Ascending cavagram confirms normal IVC.



A B

Fig. 8.

Intraosseous venogram. There is apparent filling defect at the lower end of the inferior vena cava. The lumbar veins also fill. (b) Per femoral venogram (same patient as 8a). The iliac veins and inferior vena cava are shown to be normal.

RNV detected larger calf thrombi (those in tibial veins and greater than 5 cm in length) in 20 out of 25 cases (80%). Persistence was noted in 15 (60%).

In the femoral region, 12 out of 13 (92%) thrombi were detected by RNV (Figs.2 and 3). The one case where RNV failed was that of a 5 cm non-occlusive thrombus localized to the lower femoral vein, with normal deep veins above and below it.

Group II—after seven days heparin treatment (Table II)

This group excludes any minor calf thrombi, as these are not treated with heparin. RNV detected 12 out of 14 (86.7%) thrombi; persistence was noted in eight (57.1%).

Group III—after three months treatment with warfarin (Table II)

RNV detected nine out of 23 (39.1%) thrombi; persistence was noted in four (17.4%).

Group IV—patients without DVT being assessed prior to varicose-vein surgery

RNV was falsely positive in five out of 16 (31.2%) due to persistence of isotope in superficial veins.

Group V—the proximal deep venous system

Sixteen patients with proximal occlusions were studied specifically to assess the iliac veins and inferior vena cava. RNV gave a clearer outline of the iliac veins and lower cava than XRV but the test was especially useful for monitoring the progress of patients undergoing thrombolytic therapy (see Figs. 4, 5 and 6) and clarifying confusing X-ray appearances in the inferior vena cava (see Figs. 7a, b, c).

Discussion

In patients with complete occlusion of the proximal femoral vein, ascending contrast venography

(XRV) often fails to give adequate information about the patency of the iliac veins and the presence or absence of fresh thrombus (Fig. 2). This is of great importance in the assessment of the efficacy of treatment of these thrombi and in the determination of the length of treatment with thrombolytic therapy.

There are three main alternative forms of investigation in common use, applicable to this situation. The per-femoral "Seldinger" venogram, the trans-trochanteric venogram and the retrograde venogram, performed via direct jugular puncture.

The per-femoral venogram has the obvious disadvantage of being invasive and is particularly dangerous in those cases where partially attached femoral thrombus may be dislodged by the procedure. It suffers from the added drawback that direct femoral puncture is not possible when there is total occlusion of the lumen by thrombus.

The trans-trochanteric approach has been advocated (Lea Thomas and Fletcher, 1967) but is invasive and requires the administration of a general anaesthetic. Considerable difficulties in interpretation may also be encountered (Figs. 8A and B). The retrograde approach via the jugular vein is well known and may easily be performed at the same time as pulmonary angiography. However it is also invasive and, as with the trans-trochanteric method, liable to misinterpretation (Fig. 7A, B, and C).

There is therefore a need for a simple, non-invasive method of assessing the deep venous system proximal to an occlusion. Radionuclide venography (RNV) appears to fulfil most of these criteria. First described in 1969 by Webber, RNV has undergone preliminary evaluation in several centres. The initial results have been encouraging but it has not yet become accepted as a routine diagnostic procedure. The purpose of this study was to establish its value as an addition to XRV in proximal venous occlusion and so evaluate its role in clinical practice by direct comparison with XRV.

RNV was found to be a useful addition to XRV in the upper thigh and pelvis. In 11 of 16 patients with occlusion of the femoral or iliac veins (or both), conventional ascending venography (XRV) failed to demonstrate the deep venous system proximal to the occlusion, because it was not possible to obtain an adequate concentration of contrast medium in these veins. RNV however suffered from no such disadvantage, as when the passage of radionuclide was slowed or diluted due to occlusion or collateral circulation even better γ-camera images were produced than those obtained when the radionuclide was more rapidly traversing normal veins. In the presence of occlusion RNV gave pelvic venous images not obtainable with XRV.

The overall correlation between RNV and XRV was 72%. Most of the discrepancy was due to poor correlation in the calf, especially with minor thrombi, and the occurrence of false positive results in almost one fifth of cases. However, when only those calf thrombi requiring treatment (those greater than 5 cm in length in the tibial veins) are considered, RNV detects 80%. In the femoral region, only one thrombus was missed, giving a correlation of 92%.

The basic mechanism of action of RNV has been the subject of considerable debate. The initial studies (Webber *et al.*, 1969) demonstrated uptake of isotope in the region of thrombophlebitis in the arm suggesting that MAA or microspheres directly labelled thrombus. This hypothesis was supported by *in vitro* studies (Webber *et al.*, 1974) demonstrating adherence of MAA to blood clots. These findings were further corroborated by reports of abolition of persistence of isotope by heparin (Hayt *et al.*, 1977). Later, good correlation between hot spots and "tagged" thrombi was reported in the clinical situation (Henkin *et al.*, 1974) and adherence to presumed endothelial damage at the site of femoral vein puncture demonstrated (Vlahos *et al.*, 1976). However, it has now been suggested, following *in vitro* studies, animal experiments and observations on humans, that persistence of radionuclide is more a result of venous stasis distal to an acute occlusion than true adherence to thrombus (Ryo *et al.*, 1976).

We have investigated this phenomenon in patients with incompetent perforating veins but no evidence of DVT (group IV) and also in those with thrombosis, comparing the radionuclide scans obtained immediately before treatment (group I), after seven days heparin therapy (group II), and after three months oral anticoagulation (group III).

Persistence was seen in 50% of group I, 57% of group II, 17.4% of group III and 31.2% of group IV. Persistence usually occurred distal to the area of thrombus, suggesting a mechanical obstruction as the cause of the accumulation of radionuclide rather than adherence to thrombus. This was further borne out by the presence of persistence in group II (after a week's continuous heparin treatment) and especially in group IV in whom incompetent perforating veins were known to be present in the absence of thrombosis. We conclude therefore that there is no evidence that $^{99}Tc^{m}$ MAA directly and consistently labels thrombus. It is interesting to note that in three out of the four cases where XRV was normal in the presence of a positive FUT, RNV showed persistence in the superficial veins (Table III), suggesting that radionuclide had accumulated distal to areas of superficial thrombosis. It is accepted that in up to one fifth of patients developing a positive FUT, no thrombus is demonstrable in the deep veins on contrast venography (Gallus, 1975). In these cases it is assumed that either subintimal fibrin deposition has occurred or thrombus has undergone rapid spontaneous lysis or that thrombus is in the superficial veins alone.

There is no ideal investigation for the diagnosis of acute DVT. The clinical features of this condition are notoriously confusing, with an accuracy of only 50% when based on clinical examination alone (Lambie *et al.*, 1970), and contrast venography remains the established diagnostic standard against which all other investigations must be compared. XRV is accurate and safe in the hands of those performing it regularly; however, it is invasive (Thomas, 1972) and there is a variable degree of discomfort for the patient together with a relatively high overall cost. Iodine sensitivity reactions may occur and the large hyperosmotic intravenous fluid load is undesirable in those patients with compromised cardiac function, although 60% W/V contrast media (1480m osmol/l) give less complications than the stronger solutions (Malins, 1978). The alternative less invasive diagnostic procedures in common use are the fibrinogen uptake test, Doppler ultrasound method and impedance phlebography. The former (Kakkar, 1977) is well suited to the screening of operative patients but requires at least 24 hours before results are available, precluding its use as an urgent diagnostic method. In addition, it fails to give information about the deep venous system proximal to the inguinal ligaments (Browse, 1972), or to indicate the morphological extent of a thrombosis.

The Doppler ultrasound technique (Milne *et al.*, 1971) detects only complete occlusions of the major veins and must be regarded as a crude screening test for massive thrombi. The impedance plethysmograph shows promise as a useful screening test (Strandness and Sumner, 1972), but even if accurate will only serve to indicate those patients requiring contrast venography.

RNV is certainly less invasive than conventional venography. Little expertise is necessary, and apart from the insertion of a fine needle into a dorsal vein of each foot the investigation may be performed by non-medical personnel. The additional information obtained by the simple change of site of injection of radionuclide from arm vein to dorsal foot vein suggests that RNV should be adopted in patients with suspected thrombo-embolism undergoing lung scintigraphy. The radiation dose from RNV appears to be very much less than that received during XRV. The dose to the lung from RNV is 1.2 rad (ICRP 17, 1969) with an estimated fetal dose in a pregnant woman of 0.025 rad. The skin dose during XRV is 6 rad for the two abdominal films alone, with an estimated fetal dose of 1.2 rad. It would seem that, with its specificity for the major veins of the pelvis, RNV should be well suited for use in suspected thrombo-embolism of pregnancy.

CONCLUSION

At the present stage of development, RNV will not replace XRV as the standard diagnostic procedure in suspected thrombo-embolism apart from those centres with scanning facilities where XRV is not available. However, RNV is a useful addition to XRV in those patients with occlusions of the major veins where conventional venography is difficult and at times confusing, and it appears to be the method of choice for monitoring the progress of patients on thrombolytic therapy for major venous thrombosis.

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REFERENCES

Browse, N. L., 1972. The I^{125} fibrinogen uptake test. *Archives of Surgery*, *104*, 160–163.

Gallus, A. S., 1975. I^{125} fibrinogen leg scanning in Fratantoni, J. and Wessler, S. (eds): Prophylactic therapy of deep vein thrombosis and pulmonary embolism. *DHEW Publication No. (NIH) 76–866*, pp. 77–99.

Hayt, D. B., Blatt, C. J. and Freeman, L. M., 1977. Radionuclide venography: its place as a modality for the investigation of thromboembolic phenomena. *Seminars in Nuclear Medicine*, *7*, 263–281.

Henkin, R. E., Yao, J. S. T., Quinn, J. L. and Bergan, J. J., 1974. Radionuclide venography (RNV) in lower extremity venous disease. *Journal of Nuclear Medicine*, *15* 171.

ICRP, 1969. Protection of the patient in radionuclide investigations. A report prepared for the International Commission on Radiological Protection Publication no. 17, 78. (Pergamon Press, Oxford).

Kakkar, V. V., 1972. The I^{125} labelled fibrinogen test and phlebography in the diagnosis of deep vein thrombosis. *Milbank Memorial Fund Quarterly*, *50*, 206–229.

1977. Fibrinogen uptake test for detection of deep vein thrombosis—a review of current practice. *Seminars in Nuclear Medicine*, *7*, 229–244.

Lea Thomas, M. and Fletcher, E. W. L., 1967. The techniques of pelvic phlebography. *Clinical Radiology, 18,* 399–402.

Lambie, J. M., Mahaffy, R. G. and Barber, D. C., 1970. Diagnostic accuracy in venous thrombosis. *British Medical Journal, 2,* 142–143.

Malins, A. F., 1978. Pulmonary oedema after radiological investigation of pheripheral occlusive vascular disease. *Lancet, 1,* 413–415.

Milne, R. M., Griffiths, J. M. T. and Gunn, A. A., 1971. Postoperative deep vein thrombosis. *Lancet, 2,* 445.

Ryo, U. Y., Colombetti, L. G., Polin, S. G. and Pinsky, S. M., 1976. Radionuclide venography: significance of delayed washout; visualization of the saphenous system. *Journal of Nuclear Medicine, 17,* 590–595.

Strandness, D. E. and Sumner, D. S., 1972. Ultrasonic velocity detector in the diagnosis of thrombophlebitis. *Archives of Surgery, 104,* 180.

Thomas, M. L., 1972. Phlebography. *Archives of Surgery, 104,* 145–159.

Vlahos, L., MacDonald, A. F. and Causer, D. A., 1976. Combination of isotope venography and lung scanning. *British Journal of Radiology, 49,* 840–851.

Webber, M. M., Bennett, L. R., Cragin, M. and Webb, R., 1969. Thrombophlebitis—demonstration by sciniti-scanning. *Radiology, 92,* 620–623.

Webber, M. M., Pollak, E. W. and Victery, W. K., 1974. Thrombosis detection by radionuclide particle (MAA) entrapment: correlation with fibrinogen uptake and venography. *Radiology, 111,* 645–648.

Book reviews

Positioning and Technique Handbook for Radiologic Technologists. By S. B. Conte and D. H. Kemme, pp. xiii+259+Index, 1978 (C. V. Mosby Co., St. Louis; distributed in UK by Henry Kimpton Publishers, London), £7·15.
ISBN 0-8016-1031-1.

Written by two technologists this pocket size paper-back book is a simple elementary introduction into basic radiographic techniques. The authors in their preface write "basic text books serve to introduce the essential knowledge required for quality performance, but more definite reference works must be accessible to provide the detailed information that exceeds the purpose of the text book". The book makes no pretentions to be any more than an introduction into its subject.

In its 265 pages the book is divided into 13 sections, each one concerned with the radiographic positioning of a particular system, or anatomical region. Sections 1 to 8 deal with the bony skeleton, and 9 to 12 with myelography, the digestive and urinary systems, and mammography. The final section has 46 pages under the title of positioning of cerebral, cranial and facial bones.

The format is interesting in that each page is perforated and punched to enable the reader to remove pages or sections and insert them in a binder. Each position is demonstrated by an appropriate photograph and this visual presentation is the book's main strength, although the reviewer found the variety of facial expressions of the model a detraction. The use of personalized views with their descriptive projections is a feature of the text. The few radiographs reproduced are restricted to the digestive system and some contrast media examinations.

There are some photographic errors in positioning and centring particularly with extremity radiography which are not clarified in the text, as are the subject–cassette positioning errors on pages 90 and 226. On page 114 two of the three photograph captions are incorrect, and on page 190 the anterior oblique view is confused with posterior oblique projection.

Easily read, this interesting book provides an introduction into simple radiographic positioning. Its attraction is the space provided after each projection is described and illustrated for the reader to enter his own notes and comments, and thus build up a personal radiographic technique notebook.

P. J. Richardson.

Bone tumors, General Aspects and Data on 6221 Cases (3rd edition). By D. C. Dahlin, pp. xii+445, illus., 1978 (Charles C. Thomas, Springfield, Illinois, U.S.A.), $32.75.

Bone tumours are notoriously perplexing lesions and continue to present commanding problems in both diagnosis and management. The wide variety of described entities and the rarity of some serve to compound the difficulties. It is therefore of immense help when an internationally recognized authority on the pathology of these tumours allows us to share his accumulated experience. Dahlin first presented his personal experience of more than 2000 consecutive unselected cases in text book form in 1957. The present, third edition, now encompasses 6221 cases.

The classification which is a modified version of that propounded by Lichtenstein, is now generally accepted. The details are presented in a clear didactic style which, at the same time acknowledges areas of difficulty and dispute. These are highlighted in carefully selected prose including, for example, "a practical working definition is to regard as Ewing's tumours those highly anaplastic, small round to oval cell sarcomas that have the clinical and roentgenographic characteristics of a primary osseous lesion".

There are invaluable histograms in each chapter depicting the age distribution and sites of occurrence of each tumour. The illustrations of histology are in black and white but are clear and readily comprehensible to the non-pathologist.

This volume is in no sense a treatise on the radiological investigation and appearances of bone tumours. The Author naturally holds the view that histology and cytology must be the final arbiter in diagnosis and the radiological content of the book is essentially limited to these features which are obvious to an experienced histopathologist. The illustrations of radiographs are uniformly poor and there is no mention of the role of more sophisticated radiological investigations.

Fundamental to any consideration of bone tumours is an accepted classification with specific definitions. These are presented in such a lucid way in this book that it is virtually obligatory reading for all radiologists who see or may see bone tumours. It should be perused by students preparing for Fellowship. As it is remarkably cheap, it should be acquired immediately for inclusion in the libraries of all working departments and teaching units.

John Roylance.

1979, *British Journal of Radiology*, *52*, 302–307

Whole body electron therapy in mycosis fungoides — a successful translational technique achieved by modification of an established linear accelerator

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ABSTRACT

A translational technique, adapting an established MEL SL75/10 linear accelerator, which gives a satisfactory physical and clinical 3 MeV whole-body electron treatment in mycosis fungoides is described. Tolerance of the patients proved excellent and 16 out of 21 achieved satisfactory remission of the disease. In spite of delivering significant skin doses it was possible to re-treat two relapsing patients without complications and with clinical success.

Mycosis fungoides, in its generalized forms, presents a difficult management problem. The clinical substantiation of the theoretical benefits of low-energy whole-body electron treatments was reported from the Lahey Clinic in 1962 (Smedal *et al.*, 1962), and since that time centres both in the United States (Grollman *et al.*, 1966; Fuks and Bagshaw, 1971; Miscre *et al.*, 1973) and in the United Kingdom (Bratherton, 1972; Szur, 1975) have developed different techniques and applied them with success to the disease. This paper describes a successful modification of established equipment at the Christie Hospital and the clinical results achieved with the first group of patients treated by this technique.

DESCRIPTION OF TECHNIQUE

The present technique is not different in principle from those described by Haybittle (1964) and by Trump *et al.*, (1953) in which the patient is moved relative to a beam of low energy electrons. The electron energy chosen, nominally 3 MeV, is the lowest available from the MEL SL75/10† accelerator. The patient to be treated lies on a specially constructed couch which is motor driven through the fixed electron beam at a speed proportional to the instantaneous dose rate. The circuitry required for control of couch speed is identical with that provided for control of gantry speed during rotational therapy. The couch is constrained to move along a fixed line by a mono-rail system consisting of a rail along the underside of the couch which runs between guide bearings fixed to the floor. The surface height of the couch is adjustable so that the mean SSD can be set to 1.30 m, this adjustment allowing for variation of the patients' thickness. The only modifications that have been necessary to the linear accelerator are the switching of the power supplies for the gantry rotation motor to the couch drive motor and the inclusion in the relay which performs this switching function of an interlock which allows the equipment to be operated only when the appropriate motor is connected. An additional safety interlock has been fitted to prevent accidental over-exposure of one region of the body if the movement of the couch stops for any reason. The interlock consists of a movement detector which, after an initial period of 20 seconds to allow the couch to start moving, terminates an exposure if the speed falls below a preset level (this interlock was fitted in accordance with the recommendations of the Radiotherapy Apparatus Safety Measures Panel (RASMP/75). The modifications to the accelerator are shown diagrammatically in Fig. 1.

DOSE DISTRIBUTION

The depth dose curve for the 3 MeV electron beam is shown in Fig. 2. It can be seen that a layer of tissue extending from the surface to a depth of approximately 0.9 cm can be treated to a dose greater than 80% of the maximum dose while tissues beyond 1.5 cm deep are spared.

In order to achieve uniformity of dose along the length of the patient it is necessary to move the patient through a distance sufficient that the areas treated start outside the electron beam, pass through, and finish outside the electron beam. Figure 3 shows that in practice a dose of 80% of the maximum is achieved if the patient is moved through a distance of 20 cm more than his length. Variations in uniformity also occur with changes in SSD over the patient's surface. However, variations do not follow the inverse square law. Lillicrap and Breyer, 1975, showed that for low-energy electron beams the

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†MEL Equipment Company Ltd.

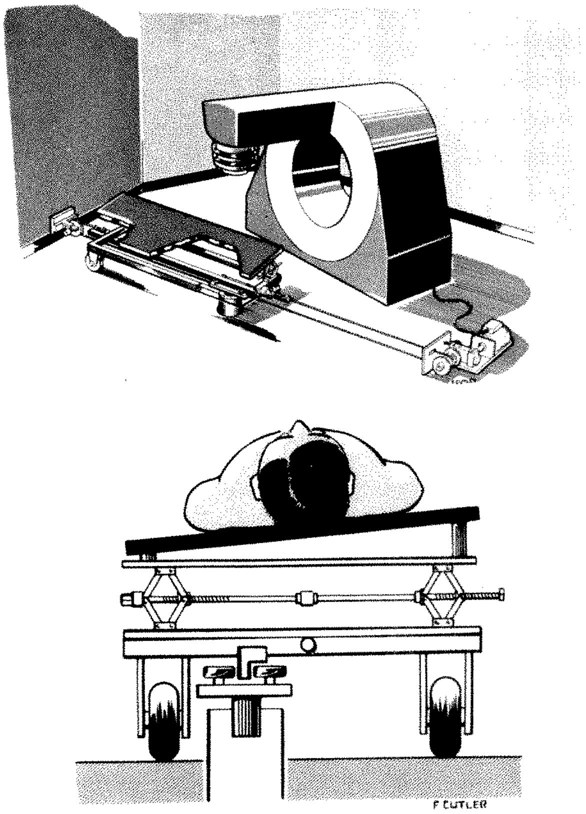

Fig. 1.
Moving couch modification to MEL SL75 Accelerator.

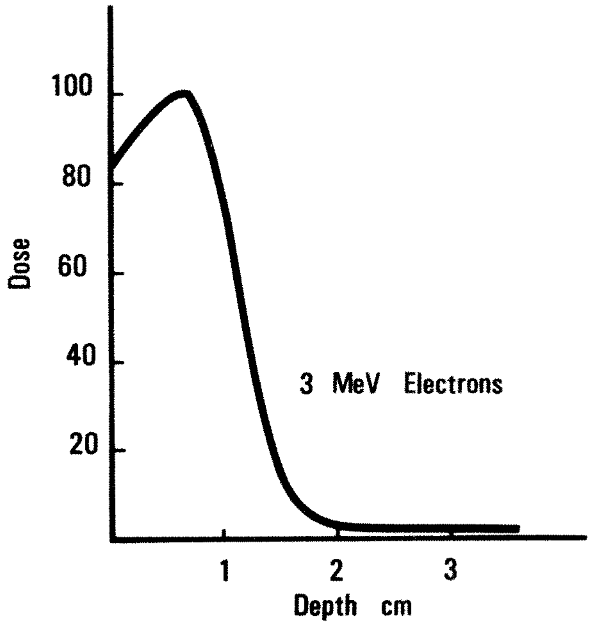

Fig. 2.
3 MeV electrons—central axis percentage depth dose curve.

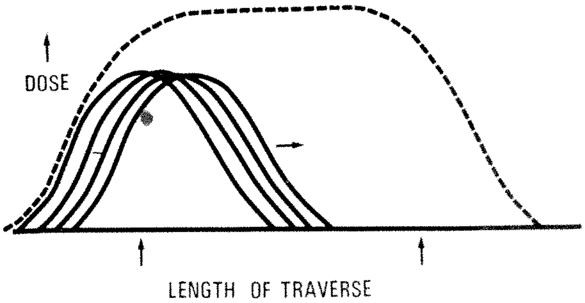

Fig. 3.
Longitudinal dose distribution obtained by translation through a fixed "Gaussian" beam.

scattering of electrons by scattering foils, collimators and by air increased the power law exponent from −2, corresponding to the inverse square law, to −2.8. They found that no universal power law could be applied, as the exponent depended on the degree to which the electrons were scattered.

In this technique no applicator is used and the X-ray collimators are fully retracted (as is necessary for operation of the accelerator in the electron mode). Measurements in fixed beams have shown that over the range 1.2 to 1.6 m SSD the variation in dose-rate follows a power law with an exponent of −2.6. However, in order to establish the variation of dose rate with SSD, measurements in a fixed beam are not appropriate to moving field techniques. It is necessary to make measurements of total dose absorbed during a full translation through the beam at each SSD. This "integration" effectively removes the divergence of the beam along the translation axis and the resultant variation in dose-rate follows a power law with an exponent of approximately one half of that measured in a fixed beam. Thus, the dose-rate in this technique is proportional to $SSD^{-1.3}$ which means that at a mean SSD of 1.3 m variations of up to 0.2 m can be tolerated before the dose falls outside the range of 80% to 120% of the mean dose.

In the plane normal to the central axis of the fixed beam at 1.3m SSD the dose distribution is approximately Gaussian and is cylindrically symmetrical about the central axis. The radial distance from the axis at which the dose falls to 50% of the dose on the axis is approximately 0.25 m. If measurements are made which "integrate" this distribution along the translation axis the transverse dose distribution is obtained; this is also Gaussian within a 50% radius of 0.25 m. The addition of two such distributions obtained by two translations through the beam centred 0.25m on each side of the central line of the patient results in a uniform distribution over a width

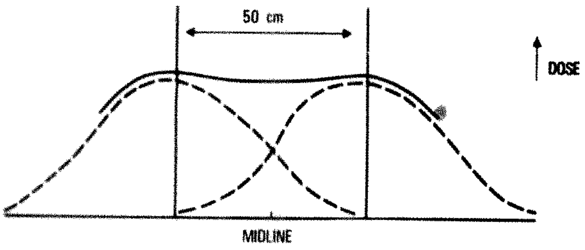

Fig. 4.
Transverse dose distribution from two overlapping fields.

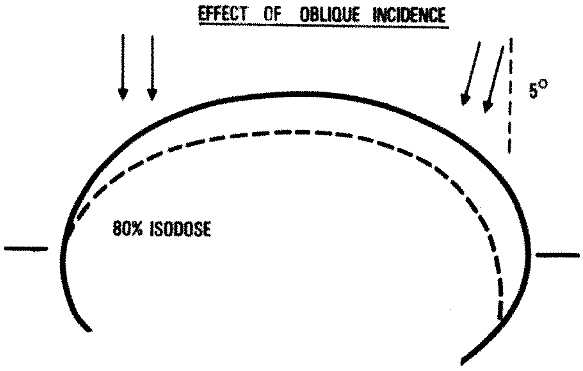

Fig. 5.
Reduction of treated depth by oblique incidence of electron beam.

of approximately 60 cm as is shown in Fig. 4. This distribution is sufficiently wide to cover most patients.

The depth dose of the treated layer, 0.9 cm at normal incidence, is reduced by oblique incidence. This reduction only becomes important at almost tangential incidence and can be avoided by tilting the patient laterally by 5 deg on the treatment couch. This also ensures that the region tangential to the beam when the patient is treated from the anterior is not tangential when the patient is treated from the posterior and vice versa (Fig. 5).

Dosimetry

Dose measurements used for this technique were based on the "Practical guide to low energy electron dosimetry", HPA Report 13 (1975), and the ionization chamber described in that report was used. The measured dose distributions have been checked both on phantoms and patients, using sachets of lithium fluoride, and have confirmed that uniform doses are achieved over the entire skin surface, except where the skin is shielded by other parts of the body, *e.g.* in the groin and axillae. The X-ray contamination has been measured to be a maximum of 2% of the electron dose in the centre of the electron beam. However, this falls to less than 1% 25 cm away from the centre of the electron beam which corresponds to the mid-line of the patient.

Dose and Fractionation Regime

The total dose is given to the patient by the addition of four fields, two from the anterior and two from the posterior. Each field is a complete longitudinal translation of the patient through the beam. The centre of the couch, and hence the centre of the patient, is offset 0.25 m from the beam axis and thus the left and right anterior fields can be treated by turning the patient round, head to feet, on the couch. Similarly the posterior fields can be treated on the same couch.

Only one of the four fields is treated each day and the week's dose to that field is delivered in a single treatment. Each patient thus has four fractions completing the whole-body treatment in one week. This is repeated on three consecutive weeks. Doses of 1600 to 3000 rad have been delivered to individual patients. The majority of patients have received 2400 rad in 12 fractions over 18 days.

Results of Treatment

Twenty-one patients have been treated during the study period. Follow-up varies from six months to four-and-a-half years (Table I). Patient 7 has been treated twice and patient 6 three times. The spectrum of clinically generalized mycosis fungoides from erythroderma to skin tumours was represented in the group. Past history varied from six months to 30 years, and in the majority of patients the histological picture was compatible with the clinical picture.

Symptomatic improvement regularly took place during treatment but objective improvements were normally noted two to four months after completion. A satisfactory response was considered to be achieved if symptomatic response and objective improvements were maintained for three months although the patient's skin did not always look completely normal. Four patients (1–4) were considered to have received no benefit from treatment and one patient (5) died of ulcerating infective complications exacerbated by his long standing paraplegia and diabetes mellitus. Satisfactory responses in the 16 remaining patients (6–21) were maintained for periods of time ranging from one to four years. Two patients (6 and 7) from this group, who relapsed with generalized disease, were successfully re-treated to full dosage. Only five patients have not required

Whole body electron therapy in mycosis fungoides

TABLE I

Details of patients including age, sex, past history, type of disease, histology and extra treatment.

Sex		Age	Past history (years)	Type	Dose (rad)	Remission length (years)	Extra treatment/complications	Histology
1	F	47	2	ulceration	1600	—		positive
2	F	71	3/4	erythroderma	1800	—		negative
3	F	45	4	Sejary's syndrome	2400	—		negative
4	F	60	1½	ulceration	2400	—		positive
5	M	62	½	patchy, plaques	3000	—	diabetic, paraplegic	positive
6	F	19	6	erythroderma	3 × 2400	⅔ 1¼ 1	superficial XRT re-treated	positive
7	M	63	30	erythroderma	1.1800/ 2.2400	4	re-treated	positive
8	M	71	7	erythroderma	2400	2	superficial XRT	positive
9	M	53	3	erythroderma	2400	3		positive
10	M	56	many	parapsoriasis	2400	½		positive
11	M	60	15	erythroderma & plaque	3000	½		positive
12	M	54	1½	erythroderma	2400	¾		positive
13	F	50	4	plaque	2400	⅔	died (lung infiltration): skin disease well	positive
14	F	54	20	tumours	2400	1¾		positive
15	F	55	several	plaques	2400	1		positive
16	M	61	2	eczema like	2400	2	superficial XRT	positive
17	M	68	4	eczema like	2400	3	superficial XRT	positive
18	F	68	2	plaque	1800	4	superficial XRT	positive
19	F	62	7	erythroderma	1600	2	superficial XRT	positive
20	M	63	7	eczema like	2400	2½	superficial XRT	positive
21	M	51	2	eczematoid	2400	1	superficial XRT	positive

further electron treatment and have maintained remissions for six months to three years after their electron treatments (8–12). One patient (13), whose skin responded satisfactorily, died of infiltrating lung disease after seven months. The eight remaining patients have relapsed but in only two has this been generalized and the remaining six have only relapsed in small patches and have been treated satisfactorily with superficial X-ray therapy at 100 kV.

Overall results

In a disease with such a variable natural history it is not helpful to express results in terms of survival. Useful objective responses have been achieved in 16 out of 21 patients.

Radiation Reactions

Skin

Only one patient (11) had a skin reaction of clinical significance on completion of a course giving 3000 rad. The reaction was erythematous on the medial surface of the thighs and settled spontaneously. No dry or moist desquamation was seen and long term skin stigmata have not been observed. No patients have developed subcutaneous fibrosis.

Appendages

Hair and nails are shed temporarily from irradiated areas. Uninvolved areas are easily shielded with 2 mm lead and can be spared clinically. In practice the eyes were routinely protected by lead spectacles, and in some patients it was possible to shield the whole head with lead. Sweat gland function continues during and after treatment and this is true of patients who have been re-treated.

Bone marrow

Bone marrow tolerance had proved excellent and is a tribute to the low X-ray contamination of the electron beam. No patient has had a significant change in haematological indices during treatment and this has been illustrated most satisfactorily by the successful completion of three full-dosage courses in two years in patient 6 (Fig. 6).

Discussion

From a radiotherapeutic point of view this technique has proved most satisfactory. Existing equipment has been modified to provide a well tolerated and reliable treatment which has produced good subjective and objective control of generalized

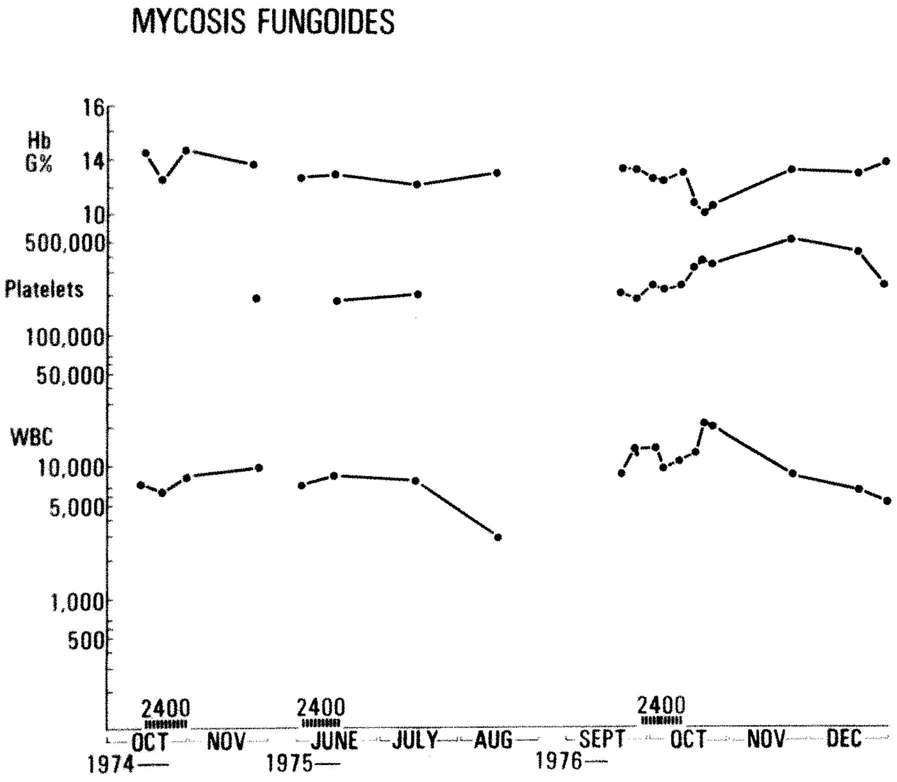

FIG. 6.

Haematological indices during and after three separate whole body electron treatments over two years in patient 6.

mycosis fungoides. Because of the complexities in contour of the human body it is not possible to achieve a homogenous dosage over all of the skin surface; the need to use superficial X-ray treatments to patches of residual disease is to be expected but in no way detracts from the usefulness of the technique. In considering other causes of treatment failure a number of points have to be reviewed. Patients in this group have received four different dose levels using this fractionation regime but the numbers involved do not permit the construction of a dose response curve. The only abnormal skin reaction was seen at 3000 rad and a disproportionate number of failures were seen at 1600 rad. The compromise of 2400 rad continues to provide satisfactory clinical results.

The physical state of the disease can present problems with this energy of electrons as the cut off is very sharp at 0.75–1.0 cm and any skin tumour thicker than this is grossly under-treated. Disease of such a type is not satisfactory for electron therapy at this energy. The physical objections to treating this type of mycosis fungoides are aggravated further by the fact that disease of this type is more aggressive and nearer the end of its natural history than the erythrodermic varieties.

The clinical experience which has come from treating this group of patients is far short of that required to define the place of whole body electron therapy in mycosis fungoides. We have no experience of treating early localized disease with this technique and cannot comment on the concept of "cure" (Fuks and Bagshaw, 1971) of the disease by early treatment. Long term control of generalized disease is, however, a reality. There is nothing about the clinical results to suggest that the responses achieved are in any way different or more successful than those reported from Hammersmith (Szur, 1975), Cambridge (Bratherton, 1972), or centres in the United States (Smedal *et al.*, 1962; Grollman, *et al.*, 1966; Miscre *et al.*, 1973). Generalized disease of the erythrodermic or eczematoid varieties can be controlled to the satisfaction of patients and doctors with minimum complications for significant and so far undefined periods of time. The responses in patients of this type are often so good and so well tolerated as to suggest that such a technique should be used in any generalized case in these early phases of the disease. Whether this influences the long term prognosis no one is in a position to say. The strength of this technique lies in the fact that worthwhile clinical results were achieved by modifications of established equipment which are physically satisfactory and safe.

REFERENCES

BRATHERTON, D. G., 1972. Strontium beam therapy. In *Modern Trends in Radiotherapy*. Ed. Deeley, pp. 176–178 (Butterworth, London).

FUKS, Z., and BAGSHAW, M. A., 1971. Total skin electron treatment of mycosis fungoides. *Radiology*, *100*, 145–150.

GROLLMAN, J. H., BIERMAN, S. M., OTTOMAN, R. E., MORGAN, J. E., and HORNS, J., 1966. Total skin electron beam therapy of lymphoma cutis and generalized psoriasis. *Radiology*, *87*, 908–915.

HAYBITTLE, J. L., 1964. A 24 cure strontium 90 unit for whole body superficial irradiation with beta rays. *British Journal of Radiology*, *37*, 297–301.

HPA, 1975. *Practical Guide to Electron Dosimetry below 5 MeV. Report 13.* (HPA, 47 Belgrave Square, London 51X 8QX).

LILLICRAP, S. C., and BREYER, B..1975. Low energy electron dose measurements on the design of large field applicators and moving field techniques. Proceedings of the 3rd International Symposium on Advances in Biomedical Dosimetry, I.A.E.A., SM–193.

MISCRE, L. Z., D'ANGIO, G. J., and KIM, J. H., 1973. Weekly total-skin electron-beam irradiation for mycosis fungoides. *Radiology*, *109*, 683–686.

SMEDAL, M. I., JOHNSON, D. O., SALIZMAN, F. A., TRUMP, J. G., and WRIGHT, K. A., 1962. Ten year experience with low megavoltage electron therapy. *The American Journal of Roentgenology*, *88*, 215–228.

SZUR, L., 1975. The treatment of mycosis fungoides and related conditions with particular emphasis on electron therapy. *British Journal of Cancer*, *31*, *Suppl. II*, 368–378,

TRUMP, J. G., WRIGHT, K. A., EVANS, W. W., ANSON, J. H., HARE, H. P., FROMER, J. L., JACQUE, G. J., and HORNE, K. W., 1953. High energy electrons for the treatment of extensive superficial malignant lesions. *American Journal of Roentgenology*, *69*, 623–629.

Book review

Breast Carcinoma. The Radiologist's Expanded Role. Editor, Wende Westinghouse Logan, 1977, pp. xv+378, illus., (John Wiley & Sons, New York/Chichester/Brisbane/Toronto)., £22·55.

In her preface, the editor states that, "Mammography offers the only hope at present of detecting breast carcinoma early enough to improve the mortality rate." So, the radiologist has a vital part to play in the early diagnosis of breast cancer. As an interpreter of images the radiologist must expand his role as a diagnostician to include a knowledge and expertise of new imaging techniques. With this in mind a conference was held at Roswell Park Memorial Institute, Buffalo, New York in October 1976 to discuss various aspects and techniques of breast imaging. This book is based mainly on a series of papers presented at this meeting. A few additional chapters are included for the sake of completeness.

The book is divided into five parts. The topics covered in each part are mainly related but there is inevitably reduplication of material in the various sections.

The first part deals with the problem of radiation induction of breast cancer, the benefits versus risks of mammography and breast cancer screening. The facts and theories are fairly presented and the overall impression is that the benefits of mammography outweigh the risks provided radiation dosage is kept to the minimum consistent with the production of a good mammographic image.

Part 2 deals mainly with some physical factors of importance in mammography. The topics include the effect of scatter, magnification technique, geometrical unsharpness, focal spot characteristics and quality control.

The third and fourth parts consider several breast imaging techniques and are extremely interesting chapters. The methods discussed include xeroradiography, film–screen mammography, magnification technique, optically enhanced mammography, electron radiography, computerized tomographic and heavy-particle mammography. It is obvious from the panel discussion that the various experts prefer their personally adopted methods. It is also clear that those with more limited experience are uncertain which of the main methods to adopt. The answer appears to be that any of the main techniques—film mammography, film–screen mammography and xeromammography give good results if well performed. The less familiar techniques have potential but require further development.

The fifth and final part contains four chapters on thermography, two recommending the technique, one concluding that the method is of no value in early diagnosis of breast cancer and the fourth describing experiments with a thermodynamic brassiere! There is an excellent article on contrast ductography but it contains an unfortunate wording on the topic of complications. If no serious complications have been encountered by the senior author what has been encountered by the junior authors? The importance of radiological control in the management of non-palpable breast lesions is well covered and there is an interesting article on a stereotaxic method of needle biopsy of non-palpable lesions. Needle aspiration biopsy of palpable lesions is described and the present status of ultrasound examination of the breast is discussed and beautifully illustrated.

The publishers are to be congratulated on the lay-out of this book. The printing and graphical work are excellent. The quality of reproduction of mammograms (which are notoriously difficult to reproduce) is superb. There are a few errors however—the mis-spelling of Gershon-Cohen's name on page 139 is unfortunate, Table I on page 154 is not one of relative skin dosages but patient statistics and the description of the patient's position for stereotaxic needle biopsy on page 313 should be "prone" and not "supine".

The overall impression is that this is an excellent book with first-class articles and up-to-date information. It is well worth reading and purchasing. It has a definite place in an academic and departmental library. It should also be found on the personal shelves of the radiologist associated with the investigation of breast disease.

I. H. GRAVELLE.

1979, *British Journal of Radiology*, *52*, 308–314

Induced thermal resistance in the mouse ear

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(*Received June, 1978 and in revised form August, 1978*)

Abstract

The mouse ear (pinna) was used to investigate the effect of two hyperthermic treatments. Heating was by immersion in hot water at 43.5°C.

A single treatment of about 50 minutes was required to cause necrosis in 50% of the ears heated. When heat treatment was given in two equal fractions the total heating time had to be increased if the interval between fractions was greater than four hours. By 24 hours a total treatment of about 100 minutes was required, indicating almost complete recovery from the first heating.

Priming treatments at 43.5°C induced thermal resistance to a second heat treatment at 43.5°C. Maximum resistance was observed one day after a 20 minute priming and two days after a 40 minute priming, when the heating time had to be increased to 120 minutes, an increase by a factor of 2.4. Shorter priming treatments induced less resistance, the minimum heating time to produce an effect being two minutes. In all cases the effect decreased during the next four to five days.

These results indicate that the reduced response of tissues to fractionated hyperthermia is due both to the repair of sublethal heat damage and induction of thermal resistance.

There is considerable experimental evidence that hyperthermia, either alone or combined with radiation or chemotherapy, may be beneficial in the treatment of some types of cancer. In order to use heat to the best advantage it is necessary to understand the response of cells and tissues to hyperthermic treatments. In clinical practice fractionated treatments are likely to be used but there is only limited information about the response of tissues to more than one heat treatment.

A few authors have reported that the response of tissues to heat alone is reduced if the heat treatment is fractionated, suggesting repair of heat damage (Moritz and Henriques, 1947; Thrall *et al.*, 1973; Suit, 1977; Hahn *et al.*, 1977). There is also evidence that the enhancing effect of heat on radiation damage is reduced if repeated heat and radiation treatments are given (Field and Law, 1978). In addition experiments on cells *in vitro* have demonstrated that heat treatment induces transient thermal tolerance. Two different phenomena have been reported. For prolonged heating at temperatures below 43.5°C there is a decrease in the slope of the cell survival curve after three to four hours (Palzer and Heidelberger, 1973; Gerweck, 1977; Harisiadis *et al.*, 1977). This effect is not observed at higher temperatures. However, if cells are heated for a short time at temperatures greater than 43.5°C and returned to 37°C for a few hours, the sensitivity to a second heat treatment is reduced (Gerner and Schneider, 1975; Gerner *et al.*, 1976; Henle and Leeper, 1976). In both cases thermal tolerance has been defined as the reduction in the slope of the heat survival curve. Such a definition is not possible for tissues *in vivo* unless cloning techniques are used. Crile (1963), however, has reported a similar phenomenon in mice. He demonstrated that a heat treatment which caused severe damage to both the mouse foot and sarcoma 180 was less effective when given 24 hours after a previous exposure to heat which itself caused little visible effect. That is, the first heat treatment induced a resistance to a second heat treatment.

Apart from the work of Crile we know of no other studies of the effect of a prior heat treatment on the response of tissues *in situ* to subsequent hyperthermia. Therefore the experiments described in the present paper were designed to investigate separately the phenomena of repair and induced thermal resistance in a normal tissue. The ear (pinna) of the mouse was chosen for this study as it is easily heated by immersion in hot water and thermal damage may be scored without difficulty. Two types of experiments were performed. In one, two equal treatments were given to measure repair of thermal damage. In the other, aimed at testing for the induction of thermal resistance, the response to a second treatment was measured at different times after a priming treatment which itself caused no visible effect.

Techniques

Female CFLP mice were anaesthetized by intraperitoneal injection of pentobarbitone sodium (Sagatal) at 0.065 mg/g body weight for hyperthermia treatments. For long treatments additional anaesthetic was required. One ear of each mouse was heated by immersion in hot water. Thermostatically controlled water baths with a temperature variation of less than 0.05°C were used and water temperatures were measured with mercury thermometers calibrated against a secondary standard. Further details of the methods are given elsewhere (Law *et al.*, 1977). All heat treatments were at 43.5°C.

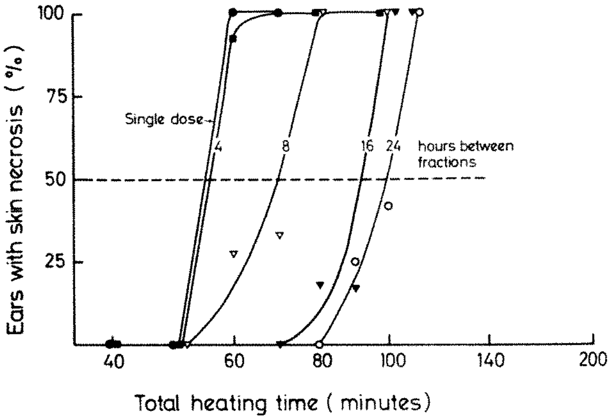

Fig. 1.

The percentage of ears developing necrosis plotted as a function of total heating time at 43.5°C given as a single treatment (●) or as two equal treatments separated by 4 (■), 8 (▽), 16 (▼) or 24 (○) hours. Each point represents a total of 6 to 12 mice.

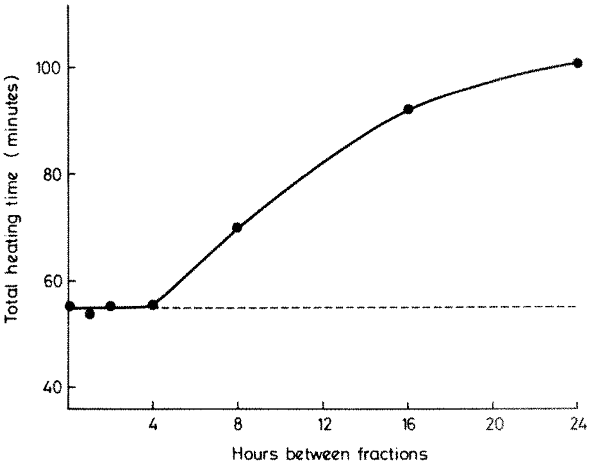

Fig. 2.

The effect of giving heat treatments at 43.5°C in two equal fractions. Total heating time required to produce necrosis in 50% of the ears heated is plotted as a function of time between fractions.

Results

Mild hyperthermia caused transient erythema in the ear. More severe heat treatment caused deep reddening and swelling which was followed by necrosis. The rate at which necrosis developed depended on the severity of the heat treatment, but it usually occurred within a few days of heating and never began after 14 days (Law *et al.*, 1978). Therefore, the response to a given heat treatment was expressed as the percentage of ears with necrosis by 14 days after heating. As soon as an ear showed signs of necrosis the animal was sacrificed.

Experiments to measure repair and induced resistance will be considered separately.

Repair

Figure 1 illustrates the effects of giving heat treatments (at 43.5°C) in two equal fractions separated by various intervals defined as the time between the end of one treatment and the beginning of the next. For each interval the total heating time was varied so that the percentage of mice developing necrosis after the second treatment ranged from zero to 100%. For all treatments, once a threshold had been reached an increase in total heating time by only 20-30% was sufficient to increase the probability of necrosis from zero to 100%. As the interval between fractions was increased the treatment time to cause a given reaction had to be increased.

The heating time required to produce necrosis in 50% of the ears heated (NT_{50}) was estimated for each time interval between treatments (Fig. 2). For a single treatment the NT_{50} was about 55 minutes. For two equal fractions no increase in total NT_{50} was required for intervals up to four hours between treatments, but for longer intervals the total NT_{50} had to be increased. By 24 hours, heating times of almost twice those required in a single treatment were needed to produce necrosis, indicating almost complete repair of the damage caused by the first fraction.

Induced thermal resistance

For two equal fractions, the total NT_{50} can never be more than twice the single treatment value because if it were the first treatment alone would be greater than the single treatment NT_{50}. This means that two equal heat treatments can only demonstrate repair. Induced thermal resistance would only be demonstrated if the NT_{50} for a second treatment given after a mild priming dose of heat were greater than the single NT_{50}. Therefore in the second series of experiments a constant first heat treatment was followed at different times by a second heat treatment whose duration was varied to produce necrosis ranging from zero to 100%.

Figure 3 shows results obtained when the first treatment was 40 minutes which is close to tissue tolerance but never alone causes necrosis. The figure gives the percentage of mice which showed signs of developing necrosis as a function of total heating time for various treatment intervals. As with equal treatments (Fig. 1), once a threshold had been reached an increase in total heating time by 20-30%

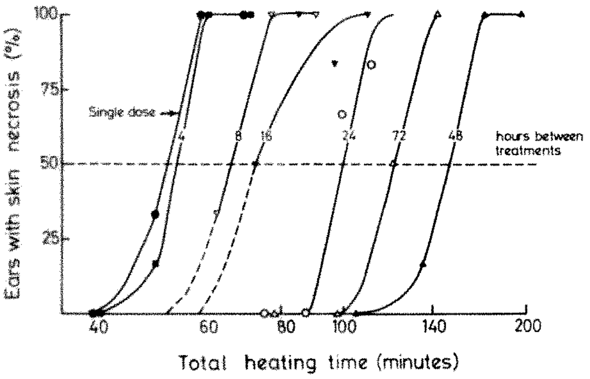

Fig. 3.

The percentage of ears developing necrosis plotted as a function of the total heating time at 43.5°C given as a single treatment (●) or as a first treatment of 40 minutes followed at 4 (■), 8 (▽), 16 (▼), 24 (○), 48 (▲) or 72 (△) hours by a second treatment. Each point represents a total of six mice.

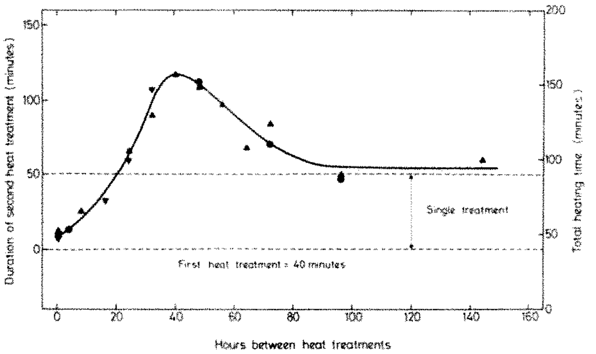

Fig. 4.

Thermal resistance induced by heating at 43.5°C for 40 minutes. The total heating time (right hand axis) or the duration of the second heat treatment (left hand axis) required to produce necrosis in 50% of the ears heated is plotted as a function of the interval between treatments. Different symbols represent different experiments. For a single treatment 50 minutes was required. A second treatment greater than 50 minutes indicates thermal resistance.

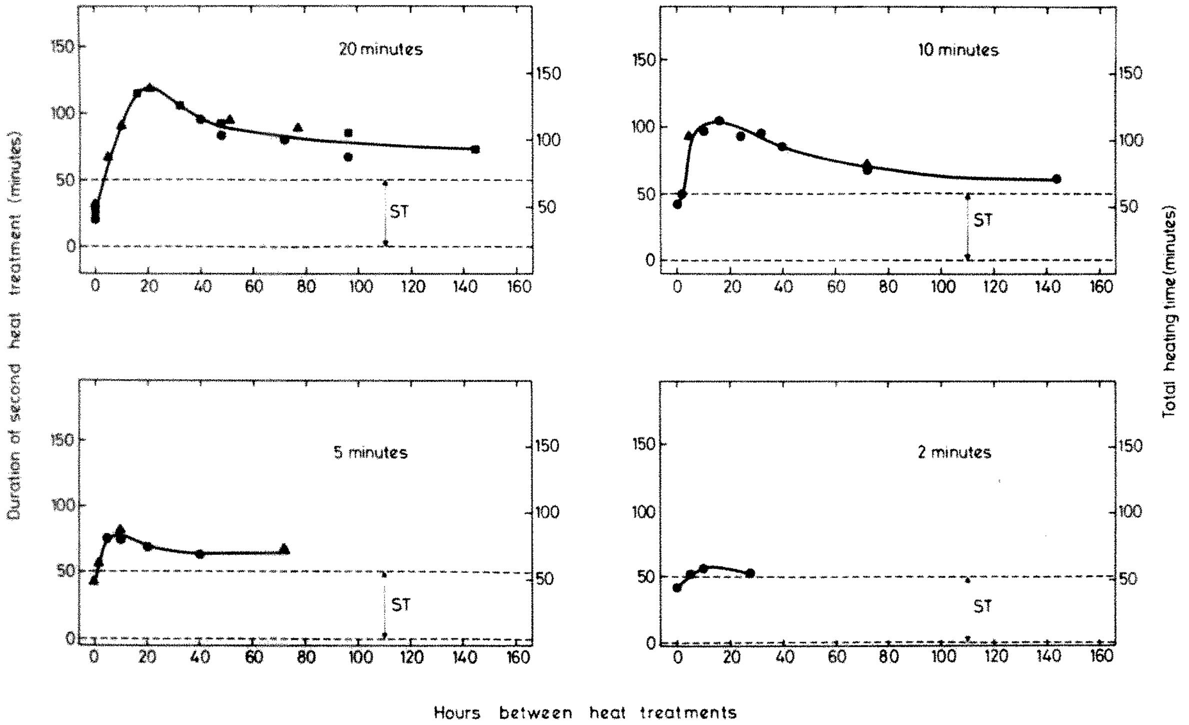

Fig. 5.

Thermal resistance induced by different heat treatments at 43.5°C. The duration of the second treatment required to produce necrosis in 50% of the ears heated is plotted as a function of the interval between treatments. First treatments were for 20, 10, 5 and 2 minutes. Different symbols represent different experiments. For a single treatment 50 minutes is required (ST). A second treatment greater than 50 minutes indicates induced thermal resistance.

increased the probability of necrosis from zero to 100%. These results are shown as isoeffect curves in Fig. 4, which shows both the total heating time required to produce necrosis in 50% of the ears heated (total NT_{50}) and the duration of the second heat treatment (second NT_{50}) as a function of the time between treatments. During the first day the results were comparable with those obtained for equal fractions shown in Fig. 2, there being little change in the second NT_{50} for intervals up to four hours after the first treatment. Subsequently the second NT_{50} increased until at 20–24 hours it was equal to the single NT_{50} of 50 minutes, an effect suggesting complete repair of the 40 minute priming dose. At longer intervals, however, the second NT_{50} increased further. This was a demonstration of induced thermal resistance. It reached a maximum at about 40 hours when the second NT_{50} was more than twice the single NT_{50}. The induced resistance subsequently decayed until by 96 hours the initial 40 minute treatment had been forgotten and the second NT_{50} was again equal to the single NT_{50}.

The effect of varying the priming treatment was then tested. In these experiments five groups of six mice were used to determine the second NT_{50} for each time interval between heat treatments. Figure 5 shows that induced thermal resistance depended on the severity of the initial heat treatment. After a 20 minute first treatment the magnitude of the effect was similar to that observed after a 40 minute treatment, but maximum thermal resistance was observed earlier. Initial treatments of ten, five and two minutes induced progressively less resistance. A one minute treatment had no effect.

DISCUSSION

Repair

No repair occurred for about four hours between heat treatments but between 4 and 24 hours it increased to a maximum (Fig. 2). These observations are consistent with results from Suit (1977) who showed little repair for five hours after treatment at 43.5°C to the mouse foot and mouse fibrosarcoma, whereas by 22 hours between heat treatments there was considerable sparing. Both results indicate that the time-course of repair after heat injury is quite different from that of repair of sublethal damage after X-irradiation which is frequently complete in about two hours (Elkind and Sutton, 1960). However Hahn *et al.*, (1977) heated mouse tails to 44°C and observed a more rapid repair than either that presented here or that found by Suit (1977), there being a measureable effect after one hour with maximum repair by 12 hours. Similar experiments *in vitro* indicate rapid repair of heat damage after treatment at 45°C, the recovery half time being one hour or less which is comparable with that after X rays (Henle and Leeper, 1976; Harisiadis *et al.*, 1977). The difference between the *in vivo* and *in vitro* results may be due to the higher temperatures used *in vitro*. Clearly the phenomenon is not fully resolved.

A further question is whether the extent of repair of sublethal damage is comparable with that after X rays. By analogy with analyses of X-ray results, the recovery after fractionated heat treatment may be expressed in terms of the average proportion of each dose recovered between fractions, F_R, given by $[(D_N - D_1)/(N-1)]/[(D_N)/(N)]$ where D_N is the total heating time required as a fractionated treatment to cause a given tissue response and D_1 is the heating

TABLE I

RECOVERED DOSE F_R

Authors	Tissue	Temperature	Single treatment	Number of fractions				
				2	3	4	5	10
This paper	Mouse ear	43.5°C	55 min	0.91				
Suit, 1977	Mouse foot	43.5°C	173 min	0.69			0.84	0.90
Suit, 1977	Mouse fibrosarcoma	43.5°C	83 min	0.83			0.80	0.86
Thrall *et al.*, 1973	Mouse mammary carcinoma	44.1°C	39 min			0.72		
Moritz and Henriques, 1947	Pig skin	49°C	9 min	>0.75	>0.75		>0.75	

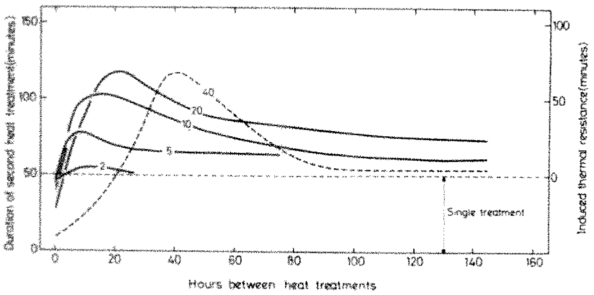

Fig. 6.

The induction of thermal resistance by different heat treatments at 43.5°C. Data from Figs. 4 and 5 are plotted to show how the duration of the second treatment required to produce necrosis in 50% of the ears changes with time after first treatments of 2, 5, 10, 20, and 40 minutes. Induced thermal resistance, defined as the extra heating time above the single treatment of 50 minutes, is indicated on the right hand axis.

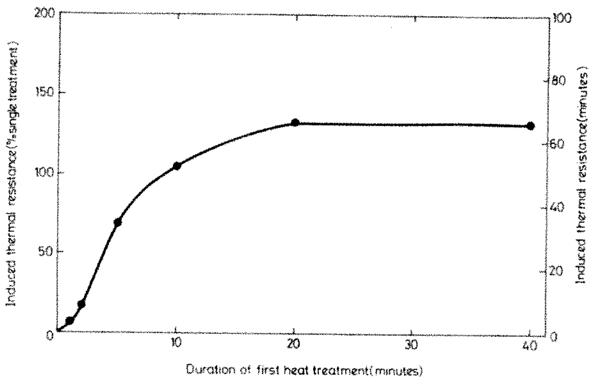

Fig. 7.

The dependence of induced thermal resistance on the severity of the first thermal treatment. Maximum thermal resistance, defined as the extra heating time above the single treatment of 50 minutes and expressed either as minutes or as a percentage of the single treatment time of 50 minutes, is plotted against the duration of the first heat treatment.

time required as a single treatment to give the same response (Denekamp, 1973). Maximum values of F_R for the mouse ear and a number of other tissues are shown in Table I. For 2–10 fractions of hyperthermia F_R ranged from 0.7 to 0.9, depending on the tissue studied. With ionizing radiation F_R generally increases from about 0.4 for two fractions to about 0.6 for ten fractions, although higher values have been obtained for larger numbers of small fractions (Denekamp, 1973; Fowler *et al.*, 1974; Denekamp and Harris, 1975). It therefore seems that tissues may have an even greater capacity to repair sublethal hyperthermic damage than radiation damage.

Induced thermal resistance

The results from Figs. 4 and 5 are combined in Fig. 6 to show how the thermal sensitivity of the ear to a second heat treatment varied with time after a number of different first heat treatments. Immediately after a priming dose of 40 minutes the ears were more sensitive to heat than if no priming treatment had been given (second NT_{50}< single NT_{50}). By 20 hours there was no apparent effect of the priming treatment (second NT_{50}=single NT_{50}) but after 20 hours the ears became resistant (second NT_{50}> single NT_{50}). Induced resistance reached a maximum at about 40 hours, after which there was a return to the situation where the second NT_{50} equalled the single NT_{50}, *i.e.* the priming dose had been forgotten. After shorter priming treatments the response was similar, but the period of induced resistance began earlier. In all cases the effect reached a maximum and subsequently decreased. These results are comparable with those obtained for other systems. For cells *in vitro* resistance is usually observed after a few hours and decays by 2–3 days (Gerner *et al.*, 1976; Henle and Leeper, 1976). For tissues *in vivo* the only results apart from those reported here are those of Crile (1963). From very limited data he reported that a treatment at 44°C for 30 minutes made the mouse foot and sarcoma 180 less sensitive to heat given 24 hours later but by 3–4 days sensitivity had returned to normal.

Induced thermal resistance may be defined as the extra heating time above a single treatment required to cause necrosis (Fig. 6). The single treatment NT_{50} varied slightly between experiments, the mean time being 50 minutes, standard deviation 4.5 minutes for nine observations. Therefore, in any one experiment the induced thermal resistance was calculated using the single treatment required in that particular experiment. Maximal induced thermal resistance, expressed either in minutes or as a percentage of the average single heat treatment of 50 minutes, is plotted as a function of heating time in Fig. 7. A 20 minute priming treatment (40% of the single NT_{50}) or longer caused the maximum effect which was 66 minutes or 130% of the single NT_{50}. Shorter priming heat treatments caused progressively less induced resistance until two minutes which caused an effect only bordering on significance. Although more severe heating has been used to induce thermal resistance *in vitro*, the magnitude of resistance in cells also decreases as the priming heat treatment is reduced (Gerner *et al.*, 1976; Harisiadis *et al.*, 1977; Leith *et al.*, 1977).

The thermal resistance illustrated in Fig. 6 could be due to a decrease in the slope of the heat survival curve, an increase in the shoulder or both. In cell lines which do not accumulate sublethal heat damage thermal tolerance is explicable in terms of decreased cell sensitivity (D_0) to heat (Gerner *et al.*, 1976; Harisiadis *et al.*, 1977), whereas in those cell lines which do have survival curves with shoulders it is due to both decreased thermal sensitivity (D_0) and increased capacity to accumulate sublethal heat damage (D_q) (Henle and Leeper, 1976). However, heat survival curves for tissues have not yet been reported.

Mechanisms of induction of thermal resistance

It has been suggested that thermal resistance might be the result of partial cell synchrony induced by the first heat treatment (Palzer and Heidelberger, 1973; Henle and Leeper, 1976). However, the time course of both induction and loss of thermal resistance is similar for cells *in vitro* with turnover times of about one day (Henle and Leeper, 1976) and in tissues *in vivo* with much longer turnover times, for example in the mouse foot (Crile, 1963) with an epithelial cell turnover time of four days (Hegazy and Fowler, 1973) and in mouse ear epidermis (present data) with a turnover time of 24 days (Sherman *et al.*, 1961). It therefore appears unlikely that induced thermal resistance is due to cell synchrony caused by the first treatment.

Two other mechanisms for the induction of thermal resistance have been suggested. First, Leeper *et al.* (1977a, b) have shown that the appearance of maximum tolerance is correlated with the recovery of protein synthesis and that incubation of cells with cycloheximide, which inhibits protein synthesis, reduces thermal resistance in proportion to the concentration of drug used. These observations suggest that thermal resistance requires synthesis of new proteins. Second, changes in lysosomes may be involved. For example, Hume *et al.* (1978) have reported two separate effects of hyperthermia on mouse splenic lysosomes. Temperatures below 42.5°C cause a transient increase in acid phosphatase activity whereas temperatures above 42.5°C cause an increase in membrane permeability. Heating the spleen induced thermal resistance for the permeability effect but not for enzyme activation, which suggests that induced thermal resistance may be connected with changes in membranes.

Clinical implications

The results in this paper and elsewhere demonstrate that cells and tissues subjected to hyperthermia show a transient resistance to further heat treatments. A report by Ludgate *et al.* (1976) suggests that this phenomenon has already been encountered in the clinic. To achieve a series of biologically equivalent "doses" of hyperthermia it will be necessary either to increase the degree of hyperthermia in the later treatments or to allow sufficient time to elapse between treatments such that the induced resistance to heat is lost. The magnitude of the induced resistance is so great that it must be taken into account in both the planning and interpreting of experimental or clinical treatments which involve repeated heat treatments. Clearly the subject requires further study.

REFERENCES

CRILE, G. Jr., 1963. The effects of heat and radiation on cancers implanted on the feet of mice. *Cancer Research, 23,* 372–380.

DENEKAMP, J., 1973. Changes in the rate of repopulation during multifraction irradiation of mouse skin. *British Journal of Radiology, 46,* 381–387.

DENEKAMP, J., and HARRIS, S. R., 1975. The response of mouse skin to multiple small doses of radiation. In *Proceedings of the sixth L. H. Gray Conference on "Cell survival after low doses of radiation: theoretical and clinical implications"*, ed. T. Alper (John Wiley & Sons, 1975).

ELKIND, M. M., and SUTTON, H., 1960. Radiation response of mammalian cells grown in culture. I. Repair of X-ray damage in surviving Chinese hamster cells. *Radiation Research, 13,* 556–593.

FIELD, S. B., and LAW, M. P., 1978. The response of skin to fractionated heat and X rays. *British Journal of Radiology, 51,* 221–222.

FOWLER, J. F., DENEKAMP, J., DELAPEYRE, C., HARRIS, S. R., and SHELDON, P. W., 1974. Skin reactions in mice after multifraction X-irradiation. *International Journal of Radiation Biology, 25,* 213–223.

GERNER, E. W., and SCHNEIDER, M. J., 1975. Induced thermal resistance in HeLa cells. *Nature, 256,* 500–502.

GERNER, E. W., BOONE, R., CONNOR, W. G., HICKS, J. A., and BOONE, M. L. M., 1976. A transient thermotolerant survival response produced by single thermal doses in HeLa cells. *Cancer Research,* 36, 1035–1040.

GERWECK, L. E., 1977. Modification of cell lethality at elevated temperatures. The pH effect. *Radiation Research, 70,* 224–235.

HAHN, E. W., FEINGOLD, S. M., and KIM, J. H., 1977. Repair of normal tissue injury from local hyperthermia. *Radiation Research, 70,* 634.

HARISIADIS, L., SUNG, D., and HALL, E. J., 1977. Thermal tolerance and repair of thermal damage by cultured cells. *Radiology, 123,* 505–509.

HEGAZY, M. A. H., and FOWLER, J. F., 1973. Cell kinetics of plucked and unplucked mouse skin. I. Unirradiated skin. *Cell and Tissue Kinetics,* 6, 517–533.

HENLE, K. J., and LEEPER, D. B., 1976. Interaction of hyperthermia and radiation in CHO cells: recovery kinetics. *Radiation Research, 66,* 505–518.

HUME, S. P., ROGERS, M. A., and FIELD, S. B., 1978. Heat induced thermal resistance and its relationship to lysosomal response. *International Journal of Radiation Biology, 34,* 503–511.

LAW, M. P., AHIER, R. G., and FIELD, S. B., 1977. The response of mouse skin to combined hyperthermia and X-rays. *International Journal of Radiation Biology, 32,* 153–161.

1978. The response of the mouse ear to heat applied alone or combined with X rays. *British Journal of Radiology, 51,* 132–138.

Leeper, D. B., Karamuz, J. E., and Henle, K. J., 1977a. Effect of inhibition of macromolecular synthesis on the induction of thermotolerance. In *Proceedings of the American Association for Cancer Research*, *18*, p.139.

1977b. Hyperthermia-induced alterations of macromolecular synthesis. *Radiation Research*, *70*, 610.

Leith, J. T., Miller, R. C., Gerner, E. W., and Boone, M. L. M., 1977. Hyperthermic potentiation: biological aspects and applications to radiation therapy. *Cancer*, *39*, 766–779.

Ludgate, C. M., Webber, R. G., Pettigrew, R. T., and Smith, A. N., 1976. Coagulation defects following whole body hyperthermia in the treatment of disseminated cancer: a limiting factor in treatment. *Clinical Oncology*, *2*, 219–225.

Moritz, A. R., and Henriques, F. C., 1947. Studies of thermal injury. II. The relative importance of time and surface temperature in the causation of cutaneous burns. *American Journal of Pathology*, *23*, 695–720.

Palzer, R. J., and Heidelberger, C., 1973. Studies on the quantitative biology of hyperthermic killing of HeLa cells. *Cancer Research*, *33*, 415–421.

Sherman, F. G., Quastler, H., and Wimber, D. R., 1961. Cell population kinetics in the ear epidermis of mice. *Experimental Cell Research*, *25*, 114–119.

Suit, H. D., 1977. Hyperthermic effects on animal tissues. *Radiology*, *123*, 483–487.

Thrall, D. E., Gillette, E. L., and Bauman, C. L., 1973. Effect of heat on the C$_3$H mouse mammary adenocarcinoma evaluated in terms of tumor growth. *European Journal of Cancer*, *9*, 871–875.

Book reviews

Radiation Effects: ESR and ENDOR Analysis. By Harold C. Box, pp. viii + 280, illus., 1977 (Academic Press, New York), £17·40.

This is a book for the specialist, either an ESR spectroscopist or radiation worker in the biological sphere.

The book divides into two parts of roughly equal length. Part I is a fairly standard account of ESR theory and techniques which should be familiar to ESR spectroscopists, but which will be useful to other radiation workers who wish to assess the results which have been obtained from the ESR and ENDOR analysis of radiation effects in biological material and to estimate what might be discovered in the future. The description of ENDOR actually occupies very few pages, in spite of the importance the author claims for it from the greatly improved resolution of spectra which it provides.

Part II describes the radiation effects which have been studied by ESR, and will be particularly useful to the spectroscopist who wishes to enter this field. The author's approach is to take a particular effect, *e.g.* oxidation, to describe this in general terms of radiation chemistry, and then to give an account of the ESR studies, usually including several by the author himself.

Dr. Box is to be congratulated on the diligence with which he has collected together the ESR studies of radiation effects; the list appears to be both complete and up to date, and the book will undoubtedly be of considerable use to the specialists mentioned above. I would not recommend it to the general reader, however, who might find the technical chapters heavy going and who, in spite of being impressed by the dedication and ingenuity of the many workers in this field, might find it difficult to decide what had been discovered that was of practical value.

There are a few minor errors—*e.g.* reference to the "Block" equations (instead of Bloch)—but nothing to cause the reader any serious problems.

S. J. Wyard.

Reconstruction Tomography in Diagnostic Radiology and Nuclear Medicine. Eds: M. M. Ter-Pogossian, J. R. Cox, Jnr., M. E. Phelps, D. O. Davis, G. L. Brownell and R. G. Evens, pp. xv + 573, illus., 1977 (University Park Press), $65.00.

This book contains the papers presented at a workshop on reconstruction tomography in diagnostic radiology and nuclear medicine held in San Juan in 1975. This Workshop took place only four years after the first computerized axial tomographic scanner was installed in the Atkinson Morley Hospital in London. In spite of this and the fact that approximately three years have passed since the time the material was prepared for publication, it is still of current interest and relevance today. The book does, in fact, represent a significant reference work in the fields of both transmission and emission computerized tomography and will find a useful place on the shelves of any physicist, mathematician or engineer working in the field.

The book is divided into three main sections: the first section containing 13 chapters or papers on the general theory of reconstruction tomography. These papers contain the bulk of the mathematical background of the subject and are the best part of the book. The middle and final sections are entitled "physical aspects" and "biomedical aspects". These contain a rather unstructured mixture of papers dealing with topics including practical problems, phantom studies, calibration and a description of reconstruction tomographic methods using radionuclides. There are, in addition, papers dealing with the problems presented by the cardiopulmonary system and some philosophical matters.

The book, although rather expensive, is well worth purchasing by physicists, mathematicians and engineers in the field and it should provide a useful reference work for research and teaching for a number of years to come.

B. R. Pullan.

1979, *British Journal of Radiology*, *52*, 315–321 APRIL 1979

The effect of prior heat treatment on the thermal enhancement of radiation damage in the mouse ear

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ABSTRACT

The effects of prior heat treatment on the skin reaction produced by a subsequent treatment with combined heat and X rays were investigated in the mouse ear. Ears were heated by immersion in hot water.

The priming heat treatment was always 43.5°C for 40 minutes. Its effect was transient, beginning between 24 and 48 hours after the priming treatment and reaching a maximum at 48 to 96 hours when there was a reduction in the skin response to combined heat and X rays, *i.e.* it caused a reduction in the thermal enhancement ratio (TER). The effect was lost by 192 hours. At 96 hours after the priming treatment the TER for 30 minutes at 42.5°C or at 43.5°C was reduced by a value equivalent to decreasing the temperature by about 0.4°C. This was equivalent to increasing the heating at 43.5°C required to produce a given enhancement of radiation damage by a factor of 1.4 relative to that required without prior heating.

The effect was smaller than induced resistance to damage caused by severe heat treatment alone (*i.e.* necrosis) and it occurred later. These differences support the concept that two separate mechanisms underlie direct heat necrosis and thermal enhancement of radiation damage.

Recent experiments with animals have shown that heat causes two qualitatively different effects in normal tissues. Severe heat treatment causes necrosis during the first few days after heating whereas moderate hyperthermia, which alone has little visible effect, enhances the response to ionizing radiation (Crile, 1963; Law *et al.*, 1978). Both these effects of hyperthermia are reduced if the treatment is fractionated (Moritz and Henriques, 1947; Suit, 1977; Field and Law, 1978; Hahn *et al.*, 1977; Law *et al.*, 1979). One explanation for these reductions is that thermal resistance is induced by the first heat treatment so that subsequent heatings are less effective. Such induced thermal resistance has been demonstrated both for cells *in vitro* (Gerner and Schneider, 1975; Gerner *et al.*, 1976; Henle and Leeper, 1976) and for tissues *in vivo* (Crile, 1963; Law *et al.*, 1979). However, there is no published information about the response of preheated cells and tissues to combined heat and radiation. Therefore the experiments described in the present paper were designed to test the effect of a priming heat treatment on the enhancement of radiation damage by a subsequent heat treatment.

The ear of the mouse was chosen for this study as the induction of thermal resistance to heat alone has already been demonstrated in this tissue (Law *et al.*, 1979). In the present experiments a priming heat dose was given at different times before a subsequent treatment with combined heat and X rays. The resultant skin reaction was compared with that after combined heat and X rays without prior heating.

METHODS

Female CFLP mice were anaesthetized by intraperitoneal injection of pentobarbitone sodium (Sagatal) for both hyperthermia and radiation treatments. One ear of each mouse was heated by immersion in hot water. Temperatures quoted are those of the water. Ears were irradiated with 250 kV X rays, HVL 1.2 mm Cu, at a dose rate of 3.6 Gy (360 rad) per minute. Irradiations were in air maintained at 25°C. Further details of the methods are given elsewhere (Law *et al.*, 1977).

RESULTS

Radiation alone caused no visible skin reaction during the first ten days but, depending on the radiation dose, erythema and then desquamation were observed after ten days. The complete reaction lasted between ten and about 50 days. When a moderate heat treatment was given immediately before or after irradiation the response to X rays was enhanced but there was no qualitative difference from the response to X rays alone (Law *et al.*, 1977).

The skin response was scored for two months after irradiation using an arbitrary numerical system. Scores of one and two indicate degrees of erythema and scores of three to nine represent increasing areas of moist desquamation (Law *et al.*, 1977). The response, either to X rays alone or when combined with mild hyperthermia, was expressed either as the maximum skin score or as the average reaction between ten and 50 days.

Experiment 1

A priming heat treatment of 43.5°C for 40 minutes was given at 24, 48 and 72 hours before a combined treatment which was 42.5°C for 30 minutes followed six minutes later by X rays. The X-ray dose was varied so that radiation dose-effect curves could be

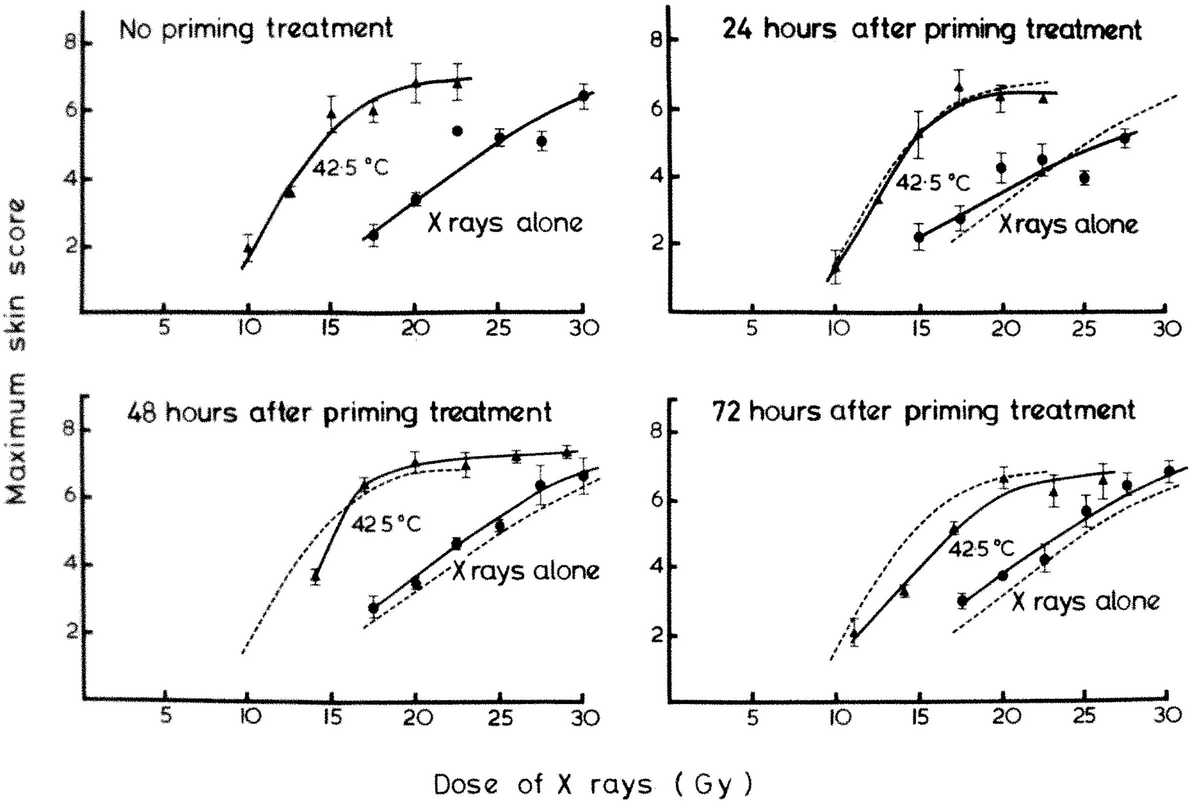

Fig. 1.

The effect of prior heat treatment on the enhancement of radiation damage by a thermal treatment of 42.5°C for 30 minutes in the mouse ear. A priming treatment of 43.5°C for 40 minutes was given 24, 48 or 72 hours before a second treatment of either X rays alone or 42.5°C for 30 minutes followed six minutes later by X rays. The results are compared with those without prior heat treatment (upper left panel and dotted lines). Each point indicates the mean for six mice and standard errors are shown.

plotted. Thermal enhancement ratios (TER), defined as the dose of X rays alone divided by the dose of X rays combined with heat to cause a given response, were calculated for each time interval between heat treatments and values, were compared with that obtained for 30 minutes at 42.5°C without prior heating. To examine whether or not the priming heat treatment used in the present experiments (43.5°C for 40 minutes) had a direct effect on the X-ray treatment, the priming heat dose was also given at 24, 48, and 72 hours before second treatments with X rays alone. In these treatments the anaesthetic was injected 10–15 minutes before irradiation.

The results are illustrated in Fig. 1. Only maximum skin scores are plotted against radiation dose but average reactions gave similar dose effect curves. Thermal enhancement ratios, calculated for both a maximum score of four and an average reaction of two, are given in Table I. The priming heat treatment did not significantly enhance the response to X rays alone. It also had little effect on the response to combined heat and radiation given at 24 or 48 hours later. However, 72 hours after the priming heat treatment the enhancing effect of hyperthermia at 42.5°C for 30 minutes was slightly reduced, the TER being about 1.5 as compared with 1.7 without prior heating.

Experiment 2

Clearly the effect of a priming heat treatment on thermal enhancement of radiation damage is small. Therefore a further experiment was performed to confirm the previous result and the study was extended to include second treatments at 43.5°C as well as at 42.5°C. The intervals between treatments

TABLE I

THERMAL ENHANCEMENT RATIOS AFTER PRIOR HEATING AT 43.5°C FOR 40 MINUTES: EXPERIMENT 1

Second treatment	Hours between treatments	Maximum score 4		Average reaction 2		Mean TER
		Dose Gy	TER	Dose Gy	TER	
X rays alone	No priming	22.0	1.00	22.0	1.00	1.00
	24	21.8	1.01	21.4	1.03	1.02
	48	21.0	1.05	21.2	1.04	1.05
	72	20.7	1.06	21.3	1.03	1.05
42.5°C, 30 min and X rays	No priming	13.0	1.69	12.4	1.77	1.73
	24	13.3	1.65	12.7	1.73	1.69
	48	14.3	1.54	13.8	1.59	1.57
	72	15.0	1.47	14.0	1.57	1.52

were also extended to test if the effects were transient, as is induced resistance to heat alone (Law *et al.*, 1979).

The results are shown in Fig. 2 and thermal enhancement ratios calculated from the data are given in Table II. Again the priming heat treatment of 43.5°C for 40 minutes had little effect on the response to X rays alone given 48 or 96 hours later. At 48 hours after priming there was little effect on the response to 42.5°C and X rays but with 43.5°C there was a reduction in TER. By 96 hours the TER with both 42.5°C and 43.5°C was reduced.

The results from experiments 1 and 2 are combined in Fig. 3 in which TER is plotted as a function of time between the priming heat treatment and second treatment. The priming treatment had little effect on the response to X rays alone but it caused a reduction in TER with both 42.5°C and 43.5°C for 30 minutes. By 96 hours the TER was reduced from 1.72 to 1.45 for 42.5°C and from 2.87 to 2.39 for 43.5°C. This result suggests that prior heating induces some form of resistance to combined heat and radiation.

Experiment 3

In order to make a direct comparison with induced resistance to heat alone (Law *et al.*, 1979), resistance to combined heat and radiation was measured in terms of the heating time required to cause a given reaction. The priming heat treatment of 43.5°C for 40 minutes was given at 48, 96 or 192 hours before a second combined treatment of 43.5°C followed six minutes later by X rays. The X-ray dose was kept constant at 9.8 Gy (a radiation dose which alone causes no visible reaction) and the duration of the second heat treatment was varied so that the radiation skin reaction varied from two to six.

The results are shown in Fig. 4. The second heating times required to produce a given skin reaction when combined with X rays are given in Table III. With no priming treatment a heating time of 23 minutes at 43.5°C given immediately before 9.8 Gy was required to give a maximum skin score of four, average reaction two. When a priming heat treatment was given at 48 or 96 hours before combined treatment, the duration of the second heating had to be increased to about 30 minutes, an increase by a factor of about 1.4. By 192 hours the effect of the priming heat treatment had been lost, a heating time of 23 minutes being required.

DISCUSSION

The results illustrated in Fig. 3 show that the TER for 30 minutes' heating at either 42.5°C or 43.5°C is reduced by a priming heat treatment of 43.5°C for 40 minutes. This reduction indicates that prior heating induces resistance to thermal enhancement of radiation damage as well as resistance to direct heat damage (Law *et al.*, 1979).

Resistance to combined heat treatment was measured in terms of the heating time required to cause a given enhancement of radiation damage (Fig. 4, Table III) so that a direct comparison could be made with resistance to heat alone. Figure 5 shows that there are differences between the two. Data for resistance induced by 43.5°C for 40 minutes were taken from Law *et al.*, (1979) for damage by heat alone and from Table III for damage by combined heat and X rays. Although both induced resistance to heat alone and to thermal enhancement of radiation damage are transient phenomena, the magnitudes and time courses of the two effects are very different. Resistance to heat alone develops by 24 hours, reaches a maximum at 48 hours and fades by 96

TABLE II

THERMAL ENHANCEMENT RATIOS AFTER PRIOR HEATING AT 43.5°C FOR 40 MINUTES: EXPERIMENT 2

Second treatment	Hours between treatments	Maximum score 4		Average reaction 2		Mean TER
		Dose Gy	TER	Dose Gy	TER	
X rays alone	No priming 48 96	21.1 19.7 20.5	1.00 1.07 1.03	21.35 20.0 19.65	1.00 1.07 1.09	1.00 1.07 1.06
42.5°C, 30 min and X rays	No priming 48 96	13.05 13.3 14.7	1.62 1.59 1.44	12.65 13.25 14.5	1.69 1.61 1.47	1.65 1.60 1.45
43.5°C, 30 min and X rays	No priming 48 96	7.35 9.3 9.2	2.87 2.27 2.29	7.45 8.55 8.6	2.87 2.49 2.48	2.87 2.38 2.39

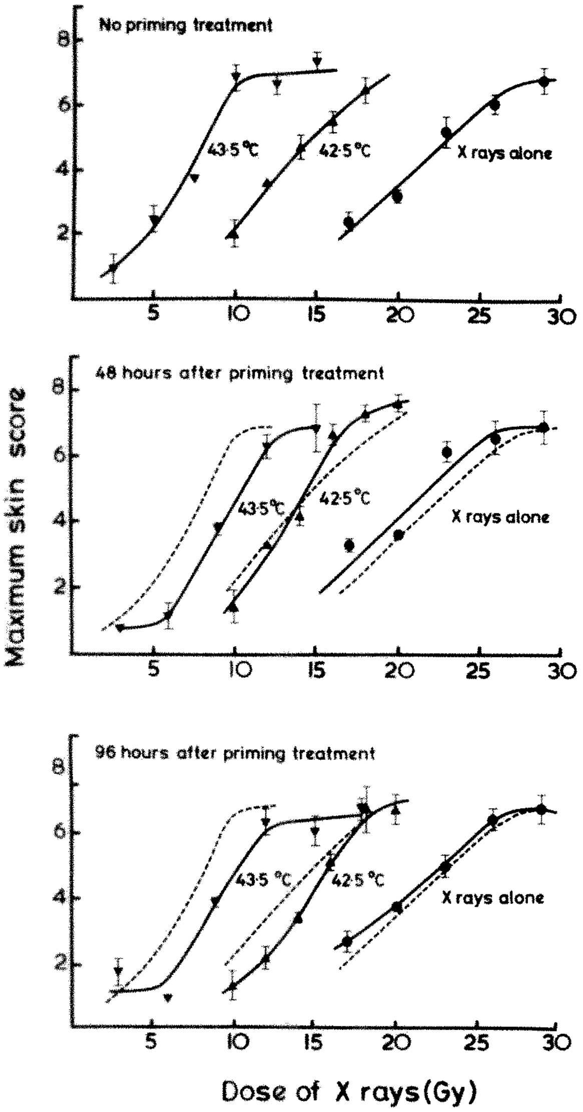

FIG. 2.

The effect of prior heat treatment on thermal enhancement of radiation damage in the mouse ear. A priming treatment of 43.5°C for 40 minutes was given 48 or 96 hours before a second treatment of X rays alone, 42.5°C for 30 minutes given before X rays, or 43.5°C for 30 minutes given before X rays. The results are compared with those without prior heat treatment (upper panel and dotted lines). Each point indicates means for six mice and standard errors are shown.

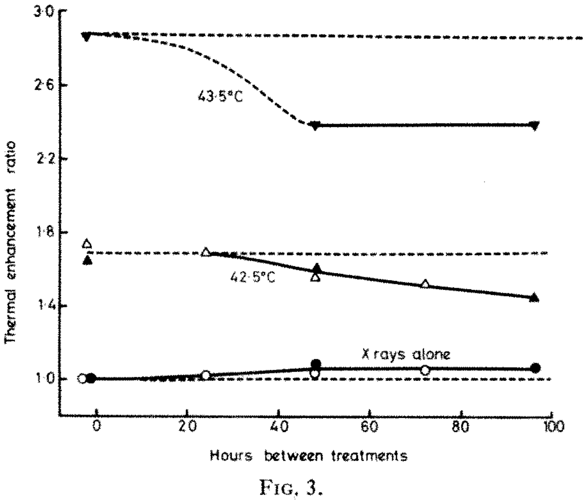

FIG. 3.

The effect of prior heat treatment on thermal enhancement ratios for the mouse ear. Mean TER's calculated for maximum skin scores of four, average reaction two, are plotted as a function of time between the priming treatment of 43.5°C for 40 minutes and second treatments of X rays alone, 42.5°C for 30 minutes given before X rays, or 43.5°C for 30 minutes given before X rays. Open symbols represent data from experiment 1, closed symbols from experiment 2.

TABLE III

The effect of prior heat treatment at 43.5°C for 40 minutes on the heating time at 43.5°C required to cause a given enhanced skin reaction to an X-ray dose of 9.8 Gy

Hours between treatments	Duration of second heat treatment			
	Minutes to give maximum score 4	Minutes to give average reaction 2	Mean duration	
			minutes	% single treatment
No priming treatment	22.6	23.6	23.1	100
48	28.4	29.6	29.0	126
96	31.0	32.0	31.5	136
192	22.4	23.6	23.0	100

hours, whereas resistance to combined heat and radiation does not develop until 48 hours, persists until 96 hours but is lost by 192 hours. At maximum resistance to heat alone, heating time has to be increased by 140% to cause a given reaction. At maximum resistance to combined treatment, heating time has only to be increased by about 40%.

The reduction in TER caused by prior hyperthermia may also be expressed as a reduction in effective temperature (alternatively to the reduction in effective heating time). This is possible because the TER is a function of temperature for a given heating time (Field *et al.*, 1977). Data from the present experiments show how the TER for 30 minutes' heating given before X rays changes as the temperature is increased from 42.5°C to 43.5°C. There are also unpublished data (Law) for the response of the mouse ear to 60 minutes' heating at 41°C and 42°C given immediately before X rays. Assuming 1°C is equivalent to a factor of 3 in heating time (Law *et al.*, 1978), 42°C for 60 minutes is approximately equivalent to 42.6°C for 30 minutes. TER's for 30 and 60 minutes' heating have been combined with the appropriate adjustment in scale in Fig. 6 to illustrate how the TER for mouse ears increases with temperature for 30 minutes. For this figure TER's have been calculated relative to X rays alone given 10–15 minutes after injection of the anaesthetic (see Law *et al.*, 1977 for discussion of the effect of anaesthesia and comparison with other tissues). Using Fig. 6, the effect of prior heating on

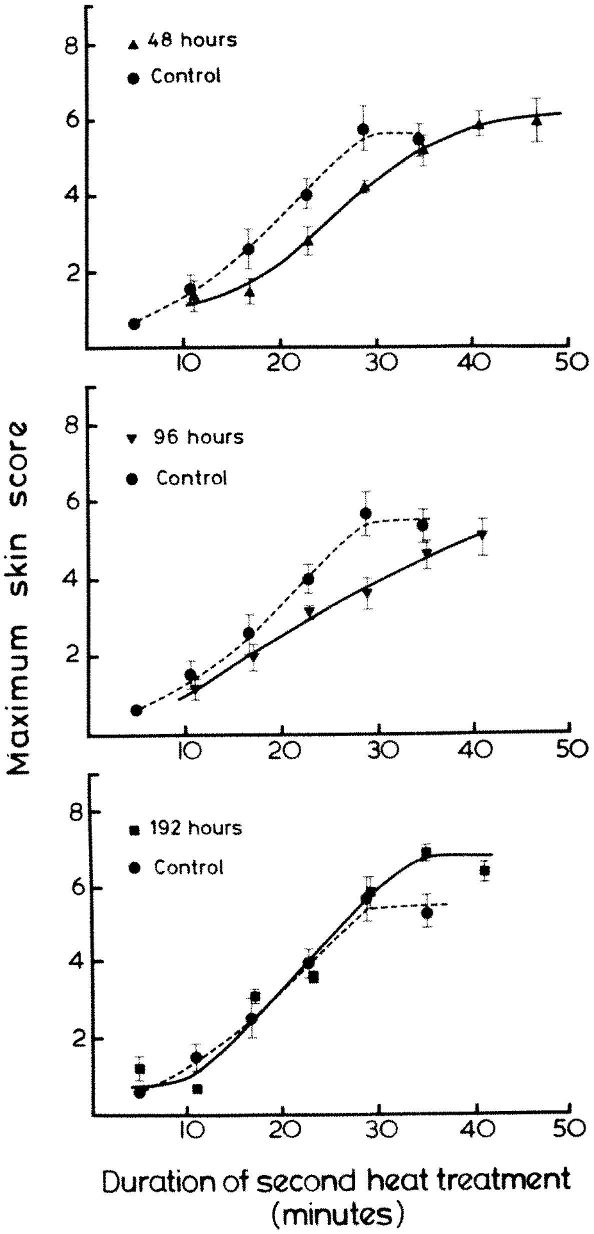

Fig. 4.

The effect of prior heating on the response of the mouse ear to combined heat and X rays. The priming treatment of 43.5°C for 40 minutes was given at 48, 96 or 192 hours before a second heat treatment at 43.5°C followed by an X-ray dose of 9.8 Gy. The maximum skin score after combined treatment is plotted as a function of the duration of the second heat treatment. Each point represents the mean of six mice and standard errors are shown.

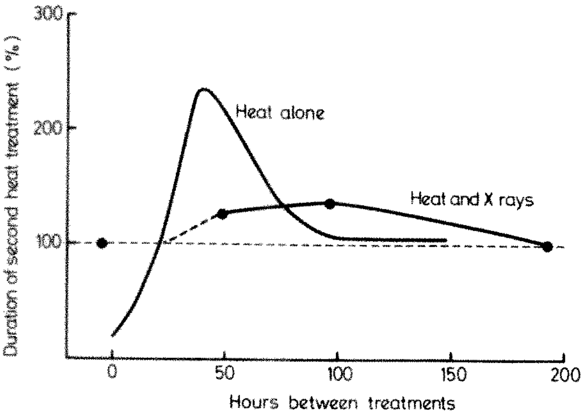

Fig. 5.

Resistance to thermal enhancement of radiation damage and to heat alone induced by a single heat treatment of 43.5°C for 40 minutes. For combined heat and radiation the duration of the second heat treatment required to give a maximum skin score of four, average reaction two, is expressed as a percentage of the duration of the single heat treatment (23 minutes) with X rays. For heat alone the duration of the second treatment required to cause necrosis in 50% of the ears heated is expressed as a percentage of the duration of the single treatment (50 minutes) (from Law *et al.*, 1979).

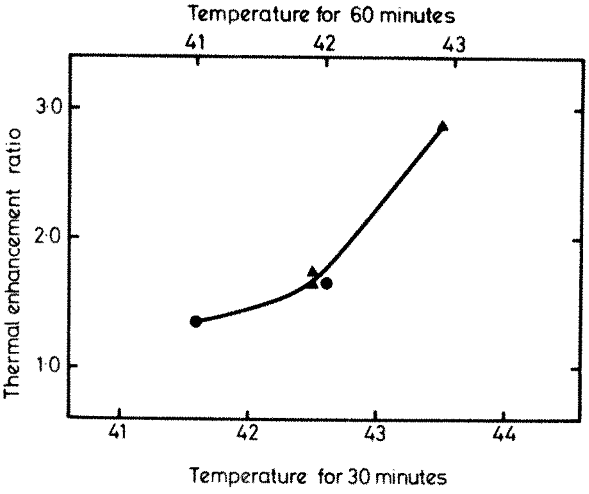

Fig. 6.

Thermal enhancement ratios for the mouse ear plotted as a function of temperature. TER's for 30 (▲) and 60 (●) minutes' heating have been combined assuming 1°C is equivalent to a factor of 3 in heating time (Law *et al.*, 1978).

the thermal enhancement of radiation damage may be expressed in terms of changes in temperature. For both 42.5°C and 43.5°C given before X rays the decrease in TER (from 1.71 to 1.45 and from 2.87 to 2.39 respectively) observed when the priming heat treatment was given 96 hours earlier (Fig. 3) was equivalent to decreasing the temperature by about 0.4°C. This suggests that by 96 hours the priming heat treatment has a comparable effect on the enhancement of radiation damage by both 42.5°C and 43.5°C for 30 minutes.

For thermal enhancement of radiation damage a change in temperature of 0.4°C is equivalent to a change in heating time by a factor of 1.5 (Law *et al.*, 1978). Therefore after a priming treatment, the duration of a subsequent heat treatment would have to be increased by a factor of 1.5 to give the enhancement of radiation damage observed without prior hyperthermia. That this is in good agreement with the directly measured factor of 1.4 (Fig. 5 and Table III) suggests that the relationship between heating time and temperature to cause a given enhancement of the radiation response is the same with and without prior hyperthermia.

The mechanisms underlying induced thermal resistance are not yet established (see review by Henle and Dethlefsen, 1978). As the cell-cycle time of epithelial cells of the mouse ear is of the order of 24 days (Sherman *et al.*, 1961) it seems unlikely that the results shown in Fig. 5 are explicable in terms of cell synchrony. Induced resistance to heat alone is related to recovery of protein synthesis after the first heating (Leeper *et al.*, 1977) but resistance to combined treatment follows a much slower time course (Fig. 5) suggesting a different mechanism. Recent experiments with mammalian cells *in vitro* have suggested that changes in membranes underlie both thermal inactivation of cells and induction of thermal resistance (Li and Hahn, 1978). Investigations by Hume *et al.* (1978a) have correlated direct heat injury with changes in the lysosomal membrane (increased permeability), in contrast to thermal enhancement of radiation damage which is related to activation of lysosomal enzymes. In more recent experiments on the lysosomal response Hume *et al.* (1978b) have shown that a priming heat treatment induces resistance to permeability changes (direct heat damage) but not significantly to enzyme activation (thermal enhancement of radiation damage). These results are comparable with those shown in Fig. 5 in which a priming heat treatment has a much greater effect on direct heat damage than on enhancement of the radiation response.

We know of no other published data pertaining to the effect of prior heating on subsequent enhancement of radiation damage. However, the close agreement between the results of the different experiments described in the present communication indicates that the effect is reproducible and is unlikely to be an artefact.

Conclusions

A priming heat treatment of 43.5°C for 40 minutes caused a reduction in the thermal enhancement of radiation damage two to four days later.

The effect was transient, with a maximum at 96 hours.

At 96 hours thermal enhancement ratios for second treatments at 42.5°C and 43.5°C for 30 minutes were both reduced by values equivalent to a decrease in temperature of about 0.4°C.

At 96 hours the heating time at 43.5°C required to cause a given enhancement of radiation damage had to be increased by 40%.

The magnitude of the effect was considerably less than the induced resistance to heat alone (after the same priming heat treatment the heating time required to cause a given level of necrosis had to be increased by 140%) and the time of the maximum effect was later. These differences suggest that different mechanisms underlie the two effects.

REFERENCES

Crile, G. Jr., 1963. The effects of heat and radiation on cancers implanted on the feet of mice. *Cancer Research*, *23*, 372–380.

Field, S. B., Hume, S. P., Law, M. P. and Myers, R., 1977. The response of tissues to combined hyperthermia and X rays. *British Journal of Radiology*, *50*, 129–134.

Field, S. B., and Law, M. P., 1978. The response of skin to fractionated heat and X rays. *British Journal of Radiology*, *51*, 221–222.

Gerner, E. W., Boone, R., Connor, W. G., Hicks, J. A., and Boone, M. L. M., 1976. A transient thermotolerant survival response produced by single thermal doses in HeLa cells. *Cancer Research*, *36*, 1035–1040.

Gerner, E. W. and Schneider, M. J., 1975. Induced thermal resistance in HeLa cells. *Nature*, *256*, 500–502.

Hahn, E. W., Feingold, S. M., and Kim, J. H., 1977. Repair of normal tissue injury from local hyperthermia. *Radiation Research*, *70*, 634.

Henle, K. J., and Dethlefsen, L. A., 1978. Heat fractionation and thermotolerance: a review. *Cancer Research*, 38, 1843–1851.

Henle, K. J., and Leeper, D. B., 1976. Interaction of hyperthermia and radiation in CHO cells: recovery kinetics. *Radiation Research*, *66*, 505–518.

Hume, S. P., Rogers, M. A., and Field, S. B., 1978a. Two qualitatively different effects of hyperthermia on acid phosphatase staining in mouse spleen, dependent on the severity of the treatment. *International Journal of Radiation Biology*, *34*, 401–409.

1978b. Heat induced thermal resistance and its relationship to lysosomal response. *International Journal of Radiation Biology*, *34*, 503–511.

Law, M. P., Ahier, R. G., and Field, S. B., 1977. The response of mouse skin to combined hyperthermia and X rays. *International Journal of Radiation Biology*, *32*, 153–161.

Law, M. P., Ahier, R. G., and Field, S. B., 1978. The response of the mouse ear to heat applied alone or combined with X rays. *British Journal of Radiology*, *51*, 132–138.

Law, M. P., Coultas, P. G., and Field, S. B., 1979. Induced thermal resistance in the mouse ear. *British Journal of Radiology*), *52*, 308–314.

Leeper, D. B., Karamuz, J. E., and Henle, K. J., 1977. Hyperthermia-induced alterations of macromolecular synthesis. *Radiation Research*, *70*, 610.

Li, G. C., and Hahn, G. M., 1978. Ethanol-induced tolerance to heat and adriamycin. *Nature* (*Lond.*) *274*, 699–701.

Moritz, A. R., and Henriques, F. C., 1947. Studies of thermal injury. II. The relative importance of time and surface temperature in the causation of cutaneous burns. *American Journal of Pathology*, *23*, 695–720.

Sherman, F. G., Quastler, H., and Wimber, D. R., 1961. Cell population kinetics in the ear epidermis of mice. *Experimental Cell Research*, *25*, 114–119.

Suit, H. D., 1977. Hyperthermic effects on animal tissues. *Radiology*, *123*, 483–487.

Book review

Roentgenology of the gall-bladder and biliary tract. Edited by B. Felson, pp. vii+150, illus., 1976 (Grune & Stratton Inc., New York). £10·30.

Radiology of the Gallbladder and Bile Ducts. By R. N. Berk and A. R. Clements, pp. xvi+407, illus., 1977 (W. B. Saunders Co., Sussex). £19·50.

Both these books are useful additions to the available literature on the gall-bladder and its diseases. Both are easily read and contain an up-to-date bibliography. The illustrations are clear—Berk and Clements textbook is the more encyclopaedic and more useful as a reference source. Students preparing for their Part I fellowship examination will undoubtedly find the chapters on gall-bladder contrast media of great value in understanding the handling and chemistry of oral and intravenous cholecystographic media. These two books should be available in all training departments.

J. A. Gleeson.

1979, *British Journal of Radiology*, *52*, 322–324

Technical note

The potential resolution of a ^{137}Cs computerized tomographic scanner for radiotherapy planning

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A number of studies have been reported of the production of anatomical cross-sections for radiotherapy treatment planning by CT scanning using simpler and cheaper detecting systems than those in the current commercial CT equipment (Webb *et al.*, 1977; Harrison snd Farmer, 1978). Although it has been shown that the location and size of inhomogeneities can be found, one of the problems of the low energy of the diagnostic X-rays used in these studies and in commercial equipment is that the linear attenuation coefficients obtained are not appropriate for the energy of supervoltage radiotherapy treatments. Additional calculation would be required to provide an accurate map of attenuation coefficients relevant to supervoltage treatment radiation. It has been suggested that the use of a source of ^{137}Cs with its γ-ray energy of 0.66 MeV might give the desired results directly (Monohan, 1977). This approach, however, has its own problems arising from the sizes and activities of possible sources and the resolution obtainable with them. These problems have been examined and some confirmatory measurements have been made with simple transmission CT equipment using ^{137}Cs.

THEORY

The theory described by Gore and Tofts (1979) has been used to estimate the limitations imposed by statistical fluctuations of photon numbers on the measurements of attenuation coefficients. The method of reconstruction employed is the filtered back-projection technique described by Ramachandran and Lakshminarayanan (1971). The standard deviation in the linear attenuation coefficient, μ, is given by the expression:

$$\sigma_\mu = \frac{\pi}{a[12.M.N]^{\frac{1}{2}}} \qquad (1)$$

where a is the pixel size in the final image and also the sampling interval in a projection, M is the number of projections and N is the number of photons transmitted per sampling interval in one projection.

The value for N_0, the number of photons from a source detected per sampling interval through a circular aperture in the absence of an absorber is:

$$N_0 = k.A.\frac{Ta}{Mx}.\frac{\pi r^2}{4\pi d^2}.\epsilon \qquad (2)$$

where k is the number of photons emitted per curie per sec; A is the activity in curies; Ta/Mx is the time per sampling interval, where T is the total scanning time, x the translational scan dimension and also the diameter of a cylindrical absorber placed in the field; r is the radius of the detector aperture, d the source-to-detector separation and ε is the detector efficiency. If the desired spatial resolution in the final image is defined by the detector aperture, r may be considered proportional to a. If, for practical convenience, the area of the detector aperture and the area of the pixel in the final image are equated, then πr^2 in equation (2) may be replaced by a^2.

Also:

$$N = N_0 \exp[-\mu x] \qquad (3)$$

Equations (1) to (3) give:

$$A = \frac{3.56 \times 10^{-3}}{\sigma_\mu{}^2.a^5.T.} \qquad (4)$$

where d is 80 cm, ε is 0.7, x is 40 cm and μ is 0.085 cm^{-1}, the linear attenuation coefficient of water at 0.66 MeV (Johns and Cunningham, 1971).

THEORETICAL RESULTS

Figure 1 shows the dependence of σ_μ/μ, the fractional standard deviation in μ, on the source strength and pixel size when the total scanning time is 20 minutes, both for idealized point sources of ^{137}Cs and for real sources with the active diameters currently available (Amersham, 1977/78). A parallel beam of radiation has been assumed resulting in a reduction in the effective activity of the sources by a factor equal to the ratio of the areas of the beam defining aperture and the source. The deviation of the dotted line from the solid line in Fig. 1 shows the extent of this effect for the real sources.

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It can be seen from Fig. 1 that for a given source activity a decrease in σ_μ/μ can be obtained by increasing a. For example, to resolve a density difference of 10%, which might require a σ_μ/μ of 3%, a 55 Ci ^{137}Cs source would provide a spatial resolution of 5 mm. For density differences of 3% for the same source strength the spatial resolution would be 7 mm. Density resolution is better than 1% for objects greater than 1 cm, using a 55 Ci source.

In addition to deciding on the optimum compromise between spatial and density resolution, consideration must also be given to the dose to the patient and to the mass of shielding required to reduce the leakage dose to acceptably low levels. Figure 2 shows the relationship between these factors for density resolutions of 10%, 3% and 1%. The dose calculated is the maximum skin dose to the patient at a distance of 20 cm from the source for 40 projections, which is the situation with our prototype equipment. The dose received by the patient will not necessarily be restrictive when the technique is used in radiotherapy treatment planning, since the dose will in any case be much smaller than the subsequent therapy dose, although the presence of vulnerable regions in the cross-section may make this allowance invalid.

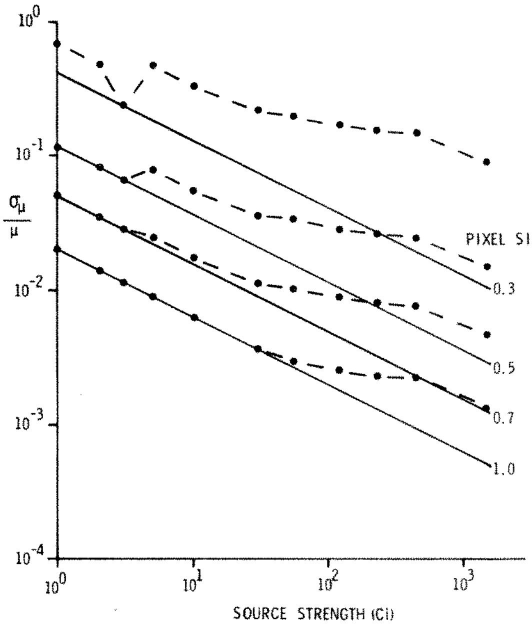

Fig. 1.

Dependence of precision in the reconstructed image on the source strength and spatial resolution. The solid lines represent the response for an idealized point source and the broken lines the response for current commercially available sources of finite size.

Results of Measurements

Measurements have been made using a prototype J. and P. dual-detector scanner modified for transmission tomography, utilizing a ^{137}Cs source, nominal activity 100 mCi, which provided a single pencil beam of radiation collimated to a diameter of 0.5 cm at the detector. Data from 40 projections of a phantom, maximum diameter 20.2 cm, containing lung equivalent material, ribs and sternum embedded in a wax material, were recorded using a Hewlett Packard mini-computer, then reconstructed using the convolution filtering technique described by Ramachandran and Lakshminarayanan (1971). A

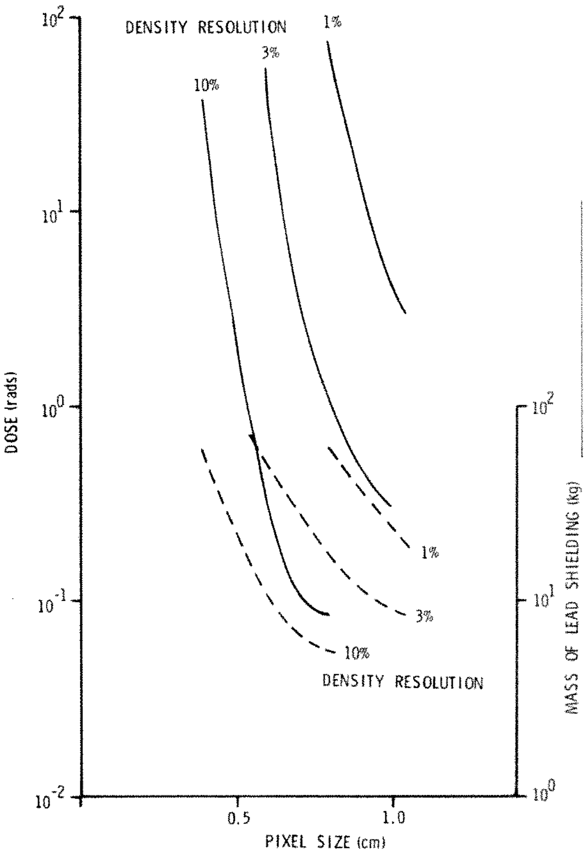

Fig. 2.

Illustration of the relationship between the maximum subcutaneous absorbed dose, the mass of shielding required for the source and the spatial resolution, for density resolutions of 10%, 3% and 1%. The solid lines represent dose and the broken lines the mass of lead in the form of a tight-fitting sphere required to reduce the dose rate of leakage radiation to 2 mrad per hour at 1 metre.

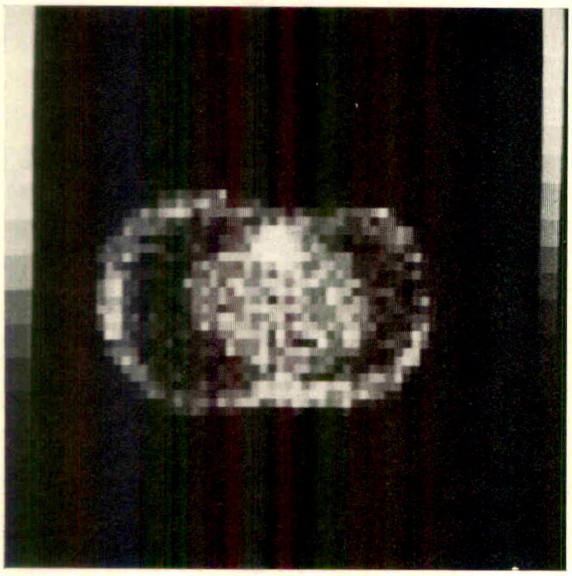

FIG. 3.

Reconstruction of a chest phantom from 40 projections. Each pixel has sides 0.52 cm and each grey level represents a change in μ of 0.0033 cm^{-1}.

sampling interval of 0.52 cm was used. From the digital printout of the reconstructed image (Fig. 3) an area was selected from the homogeneous tissue region over which the mean and standard deviation of μ were calculated, giving a value of 0.026 cm^{-1} for μ and 0.16 for σ_μ/μ. The wax material was originally designed to provide tissue equivalence at X-ray energies, consequently the measured value of μ will not resemble the expected value of μ at 0.66 MeV.

To verify the statistical theory of equation (1), the measured value for N_0 of 7.8 k counts/sampling interval was used in place of equation (2) because only nominal values were available for the activity and dimensions of the ^{137}Cs source and the detector efficiency. N, calculated from equation (3) using the measured value of μ, was inserted into equation (1), resulting in a predicted value of σ_μ/μ of 0.16, in agreement with the σ_μ/μ obtained experimentally.

CONCLUSION

It may be concluded that if ^{137}Cs is used to delineate cross-sectional tissue structure for radiotherapy treatment planning, avoiding excessive dose to the patient and a source so active that shielding becomes a problem, a spatial resolution of about 0.5 cm may be achieved. This would be adequate for treatment planning, since the position of a contour representing a change in linear attenuation coefficients covering a number of pixels could be defined with a greater accuracy than the 0.5 cm. The effect of inaccuracies in the position of edges and inhomogeneities on tumour and normal tissue dose would be acceptably small. Also, the relative positions of critical organs could be obtained by tomography with an accuracy which would provide treatment plans of greater clinical value than some presently accepted.

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I would like to thank Dr. P. S. Tofts and Dr. J. C. Gore for their most helpful discussions in the preparation of this report.

REFERENCES

AMERSHAM, 1977/78. *Radiation sources—industrial/laboratory*, p. 48–49 (The Radiochemical Centre, Amersham, Buckinghamshire, England).

GORE, J. C. and TOFTS, P. S., 1979. Statistical limitations in computed tomography. *Physics in Medicine and Biology*, *23*, 1176–1182.

HARRISON, R. M. and FARMER, F. T., 1978. The determination of anatomical cross-sections using a radiotherapy simulator. *British Journal of Radiology*, *51*, 448–453.

JOHNS, H. E. and CUNNINGHAM, J. R., 1971. *The Physics of Radiology*. Third edition, p. 746.

MONAHAN, W., 1977. Computed tomography using a Cs-137 source. *I.E.E.E. Transactions on Nuclear Science*, *NS-24*, 567–569.

RAMACHANDRAN, G. N. and LAKSHMINARAYANAN, A. V., 1971. Three-dimensional reconstruction from radiographs and electron micrographs: application of convolutions instead of fourier transforms. *Proceeding of the National Academy of Science, U.S.A.*, *68*, 2236–2240.

WEBB, S. LILLICRAP, S. C., STEERE, H. and SPELLER, R., 1977. Application of a radiotherapy simulator for imaging of body cross-sections. *British Journal of Radiology*, *50*, 152–153.

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Case reports

Diffuse infection of the spine by pseudomonas pyocyaneus

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Spinal infection arising from the paravertebral tissues is well recognized following surgery to the spine (Lowman and Robinson, 1966; Pilgaard and Aarhus, 1969). Spinal infection developing from surgery to the chest is less well known. Failure to recognize the full significance of the initial changes lead to delay in instituting correct treatment.

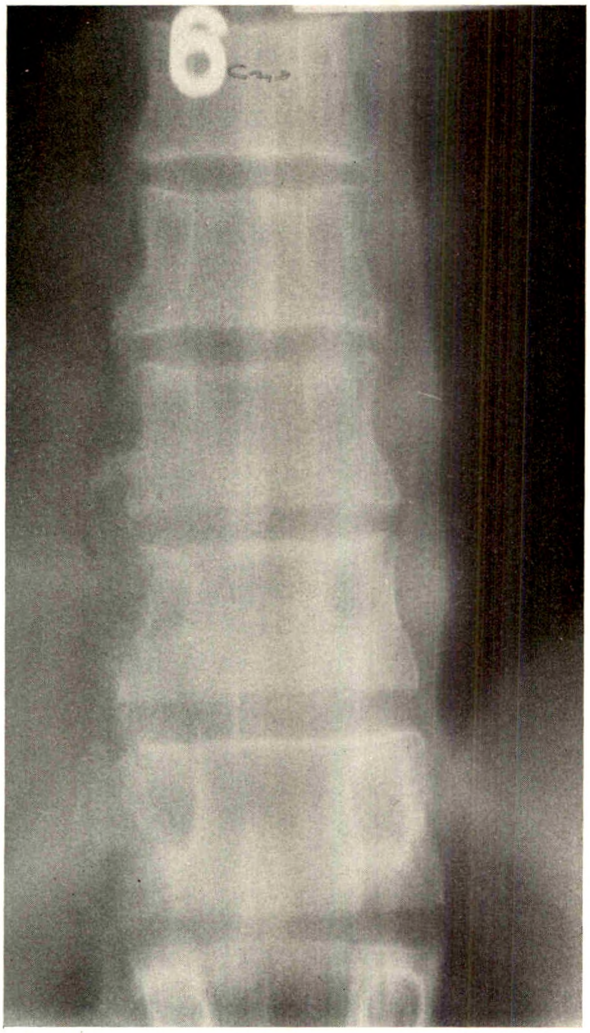

FIG. 1.
Tomographic cut demonstrating paravertebral ossification with bridging of bodies of D9–10.

CASE HISTORY

A fifty-year old general practitioner had a twenty-year history of rheumatoid arthritis. In addition to his erosive arthropathy he was found to have an enlarged liver and spleen, thrombocytopenia and leukopenia consistent with Felty's syndrome.

In March 1976, he was investigated for pneumonia and was found to have squamous carcinoma of his right lower lobe bronchus. The tumour was completely removed but his post-operative course was complicated by a wound infection. An empyema developed and although this was drained, a broncho-pleural fistula subsequently formed. This was closed by further surgery with drainage of the pleural space following the resection of the posterior parts of the right 7th, 8th and 9th ribs. Staphylococcus aureus and pseudomonas pyocyaneus were the organisms most frequently isolated from his drain.

By October, 1976 the chest had healed and he no longer required antibiotics.

He was re-admitted in November 1976 with pain in his right chest posteriorly. A polyphosphate bone scan demonstrated increased uptake in the region of the resected ribs and in the right side of T9 and T10. Tomography showed a lateral bridge of bone on the right side of T9 and T10 (Fig. 1). Needle aspiration in this region failed to isolate any organisms and the pain was ascribed to scarring around the rib resection. A chemical nerve block was performed with relief of symptoms.

In April 1977, the pain had recurred and was more severe. Radiographs on admission showed extensive lateral bony bridging from D8 to L2. The disc spaces were narrowed and the margins irregular. There was sclerosis of the affected vertebral bodies. Further needle aspiration was attempted and although no purulent material could be aspirated, following injection of saline and re-aspiration, enough material could be obtained for culture. A heavy growth of pseudomonas pyocyaneus occurred on culture.

Following five months antibiotic treatment, including Gentomycin and Carbenicillin, the infection appeared to be eradicated as judged by a decrease in pain and increase in definition of the affected vertebral bodies (Fig. 2).

DISCUSSION

Recognition of haematogenous infection of the spine presents few problems. The process beginning in the vertebral end plate leads to loss of disc space, bone destruction and sclerosis. Correlating X-ray changes with the species of infective organisms is more difficult although tuberculosis and brucella infection can show a typical pattern.

In this case, however, it seems more likely that there was contiguous spread of infection from the chest wall, probably enhanced by impaired immune response due to the patient's rheumatoid disease. The initial paravertebral new bone formation without disc space narrowing would support this concept.

1979, *British Journal of Radiology*, *52*, 326–327

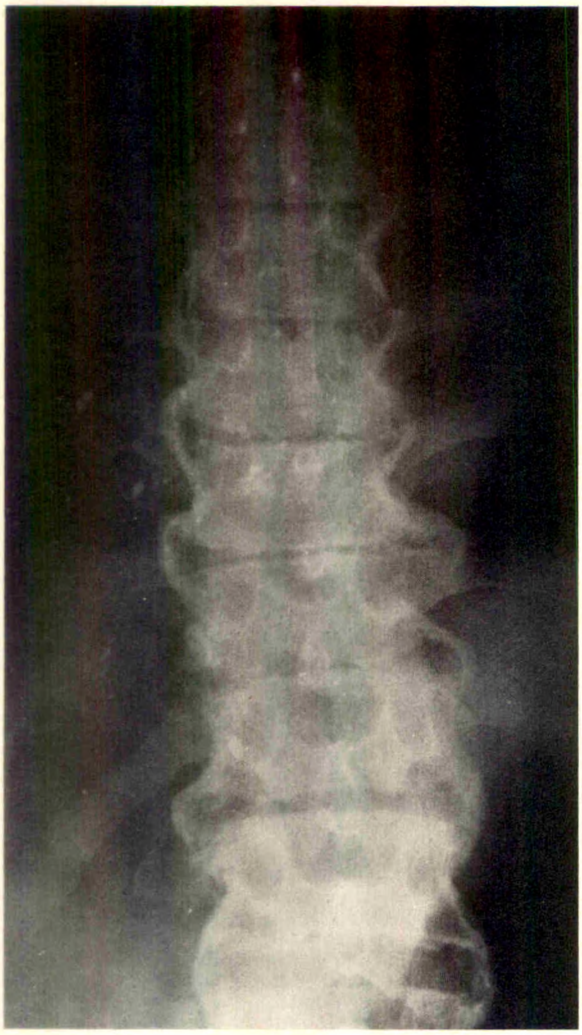

FIG. 2.

Extensive paravertebral ossification and disc space narrowing. Following chemotherapy the margins of the vertebral bodies are clearly defined.

Pseudomonas osteomyelitis is recognized as occurring in drug addicts and also as a feature of direct spread from an adjacent site of infection (Salahuddin *et al.*, 1973). Haematogenous spread of pseudomonas in the non-addict must be extremely rare.

REFERENCES

LOWMAN, R. F., ROBINSON, F., 1966. Progressive vertebral interspace changes following lumbar disc surgery. *American Journal of Roentgenology*, *97*, 664–671.

PILGAARD, S., AARHUS, N., 1969. Discitis. Closed space infection following removal of lumbar intervertebral disc. *Journal of Bone and Joint Surgery*, *51A*, 713–716.

SALAHUDDIN, N. I., MADHAVAN, T., FISHER, E. J., COX, F., QUINN, E. L., EYLER, W. R., 1973. Pseudomonas osteomyelitis. Radiologic features. *Radiology*, *109*, 41–47.

The use of percutaneous transhepatic cholangiography in a case of embryonal rhabdomyosarcoma

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(*Received August, 1978*)

Embryonal rhabdomyosarcoma (sarcoma botryoides) of the bile ducts is a tumour of mesodermal origin characterized by the growth of large polypoid mass lesions (Ackerman and Rosai, 1974). This paper describes a case of embryonal rhabdomyosarcoma arising from the common hepatic duct of a child and emphasizes the role of percutaneous transhepatic cholangiography in the management of the patient.

CASE REPORT

A four and a half-year-old female was admitted to a fever hospital with an acute onset of jaundice. She had a liver palpable two centimetres below the costal margin, and a

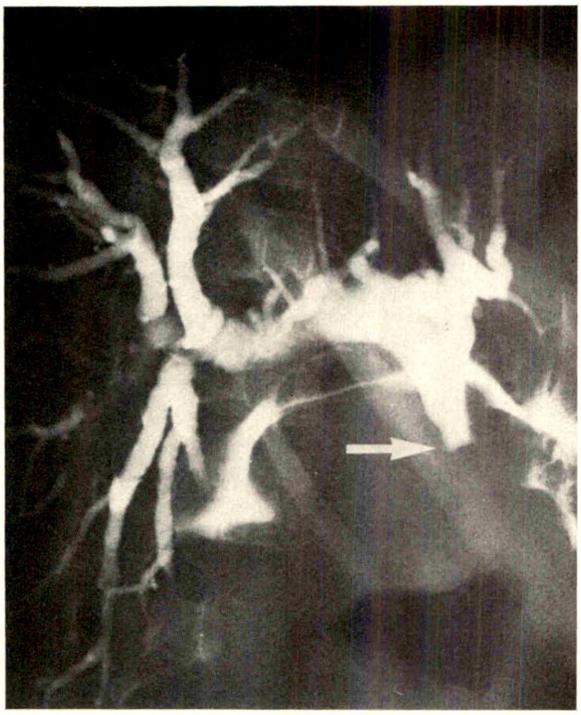

FIG. 1.

Transhepatic cholangiogram. Arrow points to totally obstructed common hepatic duct.

temperature of 37.8°C. Examination was otherwise normal. Haemoglobin was 13.4 gm/dl (13.4 gm/100 ml), white cell count $13.7 \times 10^9/1$ (13,700/mm^3), serum bilirubin 87 μmol/l (5.1 mg/d1), direct 53 μmol/l (3.1 mg/dl), SGOT 118 IU/1, SGPT 156 IU/1, alkaline phosphatase 2178 IU/1. Serum protein values were normal. The patient's jaundice increased and this was associated with a rise in both serum transaminase and alkaline phosphatase levels. Sixteen days after admission treatment with corticosteroids resulted in significant clinical improvement and a fall in the serum bilirubin value to 34 μmol/l (2.0 mg/dl). However, there was a progressive rise in serum globulin to 51 g/l (5.1 g/dl). The patient was discharged after nine weeks of hospitalization with a diagnosis of chronic active hepatitis.

Four weeks after discharge she was admitted to hospital with a history of increasing jaundice, pruritis, right hypochondrial pain, pale stools and dark urine. Her liver was now palpable five centimetres below the costal margin. Serum bilirubin was 215 μmol/l (12.6 mg/dl), alkaline phosphatase 88 IU/1, SGOT 158 IU/1, SGPT 264 IU/1, serum albumin 26 g/l (3.6 g/dl), serum globulin 43 g/l (4.3 g/dl) with raised $\alpha 1$ and $\alpha 2$ fractions. Percutaneous transhepatic cholangiography was performed and demonstrated complete obstruction of the common hepatic duct (Fig. 1). Rhabdomyosarcoma of the common bile duct was the only diagnosis suggested on these appearances.

At surgical exploration a large lobulated mass was shown involving the common hepatic duct, common bile duct, a portion of the hepatic duct and extending behind the head of the pancreas. The entire mass was excised and the common hepatic duct anastomosed end to side to a loop of jejunum. There were no obvious secondary deposits at the time of surgery. On examination the tumour measured 12×7×7 cm and was diagnosed histologically as an embryonal rhabdomyosarcoma on the findings of typical spindle shaped tumour cells with characteristic cross striations.

Since the operation the patient has been given combined chemotherapy with vincristine, adriomycin, and cyclophosphamide at two weekly intervals. She has no evidence for recurrence so far, 18 months since the operation.

DISCUSSION

Embryonal rhabdomyosarcoma of the bile ducts is a rare lesion, first documented by Wilks and Moxon in 1875. Since then 28 cases have been described in children whose ages ranged from 16 months to 11 years. The tumour has been reported in 16 females and 12 males and mean survival from time of presentation has been 5.3 months. The longest survival recorded was 16 months. Metastatic spread to lung, skeleton and lymph nodes may occur, but frequently death is due to direct extension of the tumour (Majmudar and Kumar, 1976; Sarrazin *et al.*, 1977).

Although embryonal rhabdomyosarcoma is sensitive to irradiation and chemotherapy, surgical excision is necessary to achieve a cure and therefore prompt diagnosis is essential. However, most of the cases reported were thought to have infectious hepatitis and were treated as such for a month or more (Majmudar and Kumar, 1976). As our case illustrates this must be due partially to a low index of suspicion for such a tumour, and partially to a lack of a clearcut obstructive pattern in the initial clinical history and biochemical pattern. In such instances embryonal rhabdomyosarcoma should be included in the differential diagnosis. Percutaneous transhepatic cholangiographic studies should be undertaken at an early stage of investigations if early diagnosis is to be achieved and definitive surgical treatment made possible.

REFERENCES

ACKERMAN, L. V., and ROSAI, J., 1974. *Surgical Pathology*, 5th Edition, pp. 1146–9. (C. V. Mosby Company, St. Louis.)

MAJMUDAR, B., and KUMAR, V. S., 1976. Embryonal rhabdomyosarcoma (sarcoma botryoides) of the common bile duct: a case report. *Human Pathology*, 7, 6, 705–8.

SARRAZIN, R., DYON, J. F., BRABANT, A., PONT, J., and GOUT, J. P., 1977. Sarcoma botryoide du choledoque: reflexions à propos d'un cas et revue de la litterature. *Medecine et Chirurgie Digestives*, *6*, 45–50.

WILKS, S., and MOXON, W., 1875. *Lectures on Pathological Anatomy*. 2nd Edition, Ed., Longman, Brown, Green, Roberts and Company, London, p. 465.

1979, *British Journal of Radiology*, *52*, 328–329

Case reports

Leptomeningeal aspergillosis causing internal carotid artery stenosis

By U. Kyaw Aung, M.B., B.S., D.M.R.D., F.R.C.R., U. Kyi Lin, M.B., B.S., D.M.R.D., and U. Saw Nyunt, M.D.

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(*Received July, 1978*)

Fungus infection of the leptomeninges is uncommon. Aspergillosis is known to occur in patients with debillitating disease, drug addiction, chemotherapy and following prolonged steroid treatment (Dayal *et al.*, 1974). It presents predominantly as proptosis and associated sinus disease due to involvement of the orbit and base of the skull. The diagnosis of aspergillosis of the central nervous system is rarely established pre-operatively and this case report highlights some of the difficulties.

CASE REPORT

A 22-year-old housewife first complained of headache during the eighth month of pregnancy. This was followed by retrobulbar pain and blurring of vision 22 days after delivery necessitating admission to the Department for Neurological Services. Clinical examination revealed proptosis of the left eye with complete ophthalmoplegia in a patient in obvious pain. The EEG, ultrasound and brain scan were all normal. Radiographic examination showed widening of the left superior orbital fissure with reactive basal sclerosis of the sphenoid (FIG. 1). The optic foramen was normal. Angiography revealed narrowing of the internal carotid artery with complete interruption of flow at the level of the sella (Fig. 2). A biopsy of the naso-pharynx was not conclusive.

Her condition deteriorated with worsening of the pain and proptosis. Repeat skull examination one month later showed further destruction of the orbital fissure, erosion of the optic foramen and opacity of the ethmoids. Angiography revealed more extensive narrowing of the internal carotid artery on the left. The right remained normal.

At operation, pus was aspirated from the retrobulbar space on the left and from the floor of the anterior cranial fossa. Biopsy demonstrated aspergillus involving the leptomeninges. A culture could not be obtained. The patient was treated with antifungal drugs but died almost a month later. An autopsy was not performed.

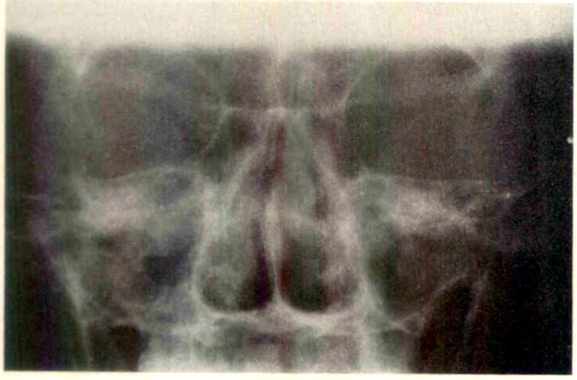

FIG. 1.

Plain film of the orbits shows normal right side and widening of the superior orbital fissure on the left side.

DISCUSSION

The presentation in this young female with exophthalmos and painful ophthalmoplegia suggested a number of possibilities. The association of orbital fissure destruction, ethmoid and sphenoid involvement and internal carotid artery occlusion suggested

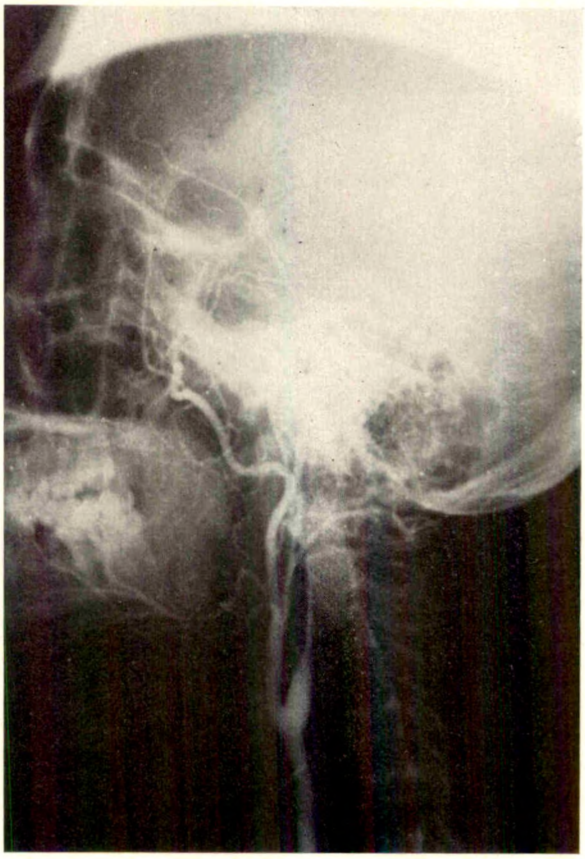

FIG. 2.

Left carotid angiogram shows narrowed internal carotid artery. The contrast medium can be visualized only to the sella.

a neoplasm. A primary carcinoma of the sphenoid sinus with secondary involvement of adjacent structures was suspected. This was not confirmed by nasopharyngeal biopsy, a situation which has been previously recorded (Taveras and Wood, 1964). Mucocoele of the sphenoidal sinus may give a similar pattern of bone destruction but is not usually associated with occlusion of the internal carotid artery.

The diagnosis was established by histological examination of the leptomeninges which showed that the hyphae were actually embedded in the arterial wall and the occlusion was due to these becoming entangled in the lumen. In this instance the fungus itself acted as a nidus for thrombosis. The angiographic demonstration of multiple occlusions and arteritis in aspergillosis has been documented (Newton and Potts, 1974).

Fungal infections are opportunistic. Cerebral infarction has been reported secondary to fungal embolism complicating aspergillous infection of aortic valve prosthesis (Kaufman *et al.*, 1976). There are few reports of intra-cranial aspergilloma. Necrotizing inflammatory vascular occlusion is usually rapidly fatal (Samuel, 1968).

Another fungus disease, mucormycosis may be seen in poorly controlled diabetics, in pregnancy and in patients undergoing chemotherapy (Hedges and Leung, 1976). Orbital and basal bone destruction may occur with venous and cavernous sinus thrombosis and occlusion or narrowing of the internal carotid artery.

REFERENCES

DAYAL, Y., WEINDLING, H. M. and PRICE, D. L., 1974. Cerebral infarction due to fungal embolus. A complication of aspergillus infection on an aortic valve prosthesis. *Neurology, 24,* 76–79.

HEDGES, T. R. and LEUNG, L. E., 1976. Parasellar and orbital apex syndrome caused by aspergillosis. *Neurology, 26,* 117–120.

KAUFMAN, D. M., THAL, L. J. and FARMER, P. M., 1976. Central nervous system aspergillosis in two young adults. *Neurology, 26,* 484–488.

NEWTON, T. H. and POTTS, D. G., 1974. *Radiology of the Skull and Brain* (C. V. Mosby Co., St. Louis.)

SAMUEL, E., 1968. Inflammatory disease of nose and paranasal sinuses. *Seminars in Roentgenology, 3,* 148–159.

TAVERAS, J. M. and WOOD, E. H., 1964. *Diagnostic Neuroradiology* (Williams and Wilkins, Baltimore.)

Book reviews

L'angiographie digestive chez l'adulte et l'enfant. By D. Doyon, A. Roche and P. Chaumont, pp. viii+182, illus., 1978 (Editions Masson, Paris), F.192.
ISBN 2-225-49380-4.

The authors of this French atlas of gastro-intestinal angiography are two radiologists and a clinician from the "Hopital de Bicêtre, Faculté de Médecine Paris-Sud." Their presentation covers all aspects of the field ranging from technique, inflammatory and neoplastic diseases to emergency angiography in digestive pathology. There is an excellent section on paediatric gastro-enterology with full discussion on the particular problems in performing angiograms on the very young. Especially impressive is the respect the authors give to the dosage of contrast media used in children and to radiation protection.

It is unfortunate for readers who are not fluent in French that the text, captions and extremely good index are completely in French. The format of each chapter consists of short discussions and tables of differential diagnoses, the emphasis being on numerous radiographic illustrations and line drawings. The radiographs are uniformly superb and it is a tribute to Gallic inventiveness that many of them are literally as small as postage stamps, yet the relevant information, be it extravasation of contrast or encasement of vessels, is clearly present.

A full bibliography of both English and French authors is included. This concludes the book, the lack of references within the individual chapters making for easier reading. A set of challenging problem exercises forms the last section of a book which could well become a best seller if it were published in languages other than French.

R. DICK.

Atlas of brain anatomy for CT scans (using EMI terminology). By F. C. Shipps, J. McAndrew Jones and A. D'Agostino, pp. vii+51, illus., 2nd edn., 1977 (Charles C. Thomas, Springfield, Illinois, U.S.A.), $16.75.

The second edition of this atlas retains the format of the first edition in which anatomical brain sections cut at 0 deg and 15 deg to the orbital meatal line in the plane of the usual CT projections, are presented with labelled plastic overlays, which are very useful for self-instruction. Comparable CT sections are mounted opposite the 15 deg angle brain sections.

The subject material has been expanded to include chapters on artefacts, absorption values and methods of localizing CT data in relation to the lateral skull film and of obtaining corresponding brain sections from autopsy specimens.

The anatomical sections are excellent, but the labelling is limited to the major structures and will be of value only to those who are commencing study of the subject. The CT sections are mainly of good quality, but a few are not up to standard and should be replaced.

The scope of a future edition could be profitably increased by including the orbit, coronal slices and perhaps sagittal reconstruction, which have a logical place in a book of this nature. There is much unused space on which such additions could be made without adding to the bulk of the volume.

The second edition of the atlas is a marked improvement on the first. Its main value is in providing anatomical sections corresponding to the usual CT slices and it is recommended for this purpose.

BRIAN KENDALL.

1979, *British Journal of Radiology*, 52, 330

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Treatment of ankylosing spondylitis

The Editor—Sir,

In an article published in The British Journal of Radiology Smith *et al.* (1977) reviewed the causes of death in a group of patients with ankylosing spondylitis who were not intially treated by X rays and compared them with a larger and not strictly comparable group who had been treated by X rays at about the same time. They concluded that the known increased incidence of malignant tumours, including leukaemia, in patients treated with X rays is due to the treatment rather than to the disease process itself, but drew attention to the possibility that the increase in deaths from malignancies in irradiated patients may be compensated, at least in part, by a reduced number of deaths from other causes when comparison is made with the mortality experience of patients treated in other ways.

The question was therefore asked yet again whether treatment by radiotherapy can be justified on the grounds that it offers the possibility of better symptomatic relief than that which follows other forms of treatment and, in particular, the suggestion was made that The British Institute of Radiology should organize a clinical trial to assess the symptomatic improvement accruing from X-ray treatment of patients with ankylosing spondylitis compared with the treatment by non-radiation methods. It was suggested that on the rather unlikely assumption that treatment with X rays reduces mortality rates by 40% compared with other methods of treatment, then it would be necessary to include about 1000 patients in a trial and follow them for ten years to be 90% certain of declaring a difference significant at the 5% level. However, a smaller number of patients would be required if the criterion of effectiveness was the relief of symptoms rather than death.

A survey of consultant radiotherapists and of radiotherapy centres was therefore carried out and replies have been received from about three-quarters (157 consultants out of 210 and 45 centres out of 60). These radiotherapists indicated that over the last three years they had treated about 340 patients with ankylosing spondylitis, though a considerable number of them thought that additional patients would be referred in the event of a trial being set up. However, at least one large centre which treated 60 patients is doubtful as to whether it would contribute to a trial, another treating 40 patients has decided not to take part, two regional centres are unwilling to contribute patients to a proposed trial and at least one major London teaching hospital feels that such a trial would not be justified.

I presented these figures to a recent meeting of the Medical Committee of the Institute with my own personal feeling that there is not enough support or potential support from radiotherapists to warrant an approach to rheumatologists and orthopaedic surgeons to enlist their support for a trial. I think it unlikely that a sufficiently large number of patients would be recruited and I further think that, as there would be at best relatively few patients from each of a large number of centres, there would be problems in collecting information and ensuring that the protocol was exactly observed.

The Medical Committee agreed with this assessment, but there would of course be no objection to any other Body looking into the matter further.

Yours, etc.,
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(*Received November, 1978*)

REFERENCE

Smith, P. G., Doll, R., and Radford, E. P., 1977. Cancer mortality among patients with ankylosing spondylitis not given X-ray therapy. *British Journal of Radiology*. *50*, 728–734.

The effective atomic number of mix D

The Editor—Sir,

It is well known that mix D, which was introduced by Jones and Raine (1949), has been widely used as a phantom material for photons and electrons in radiotherapy. By adding fillers of magnesium oxide and tianium dioxide to wax, they made an improvement for mix D compared with wax alone in terms of mechanical properties and the attenuation characteristics of photons. In their paper, they reported that "We, therefore, calculated a modified prescription to adjust the value to 7.42" and "Dr. Spiers found an experimental $\bar{Z}$-value of 7.47 for mix D".

Recently, we calculated a value of the effective atomic number ($\bar{Z}$) for mix D by using the following formula.

$$\bar{Z}=(\Sigma a_i Z_i{}^{2\cdot 94})^{1/2\cdot 94}$$

where a_i is the fractional electron content of element Z_i. We have found a $\bar{Z}$-value of 6.971 and an electron density of 3.401×10^{23} electrons per gram for mix D, of which the elemental composition was taken from the table of HPA (1977). Jayachandran (1971) reported calculated values of 7.46 and 3.395×10^{23}.

Yours, etc.,
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(*Received October, 1978*)

REFERENCES

Jones, D. E. A., and Raine, H. C. (1949). Correspondence, *British Journal of Radiology*, *22*, 549–550.

HPA 1977. Phantom materials for photons and electrons. Scientific Report Series-20.

Jayachandran, C. A., 1971. Calculated effective atomic number and kerma values for tissue-equivalent and dosimetry materials. *Physics in Medicine and Biology*, *16*, 617–623.

The calculation of effective atomic number, $\bar{Z}$.

The Editor—Sir,

Your correspondents (Hiroaka and Kawashima, 1979) are, I find, correct in stating that 6.97 is the value of $\bar{Z}$ for mix D (Jones and Raine, 1949) as calculated from the formula of Mayneord (1937), *i.e.*, $Z^{2\cdot 94}=\Sigma a_i z_i{}^{2\cdot 94}$, where a_i is the electron contribution of the element i and Z_i is its atomic number. Unfortunately, the work sheets for this 30-year-old investigation are no longer available, so that the source of the regrettable error, responsible for the then published value, 7.42, can no longer be traced. I can only surmise that, having arrived at an effective atomic number in exact agreement with that similarly calculated for water, we were too ready to accept it without further check. Moreover, Spiers's experimentally determined value for mix D (Spiers, 1946), 7.46, was in satisfactory accord with it. The fact that Jayachandran (1971) calculated the same false value by the same method adds to the "comedy of errors", as he aptly refers to it in a recent private communication.

The fact remains, however, that many workers have found mix D to be a useful substitute for water over a wide range of photon and electron energies. At the higher energy range, where photo-electric absorption becomes negligible in comparison with the Compton and electron-pair production effects, mix D would be expected to simulate water because the electron density has the correct value. How, then, can we explain the satisfactory water-equivalence at energies where the photo-electric effect is by no means negligible? If the mix D $\bar{Z}$-value is, in fact, too low by as much as 6%, the photo-electric coefficient, τ, should be about 22% less than that for water. Clearly, we must re-examine the validity of the Mayneord expression.

According to Spiers (1946), the formula is derived from Walter's (1929) empirical relationship between τ, Z and λ (the latter being the wavelength of the radiation), namely, $\tau = kZ^{3.94}\lambda^3$, and his paper shows how Mayneord's expression is derived, resulting in the exponent of Z being reduced to 2.94. I have therefore investigated the validity of the Walter formula, using much more recent data than were available in 1929. Johns and Cunningham (1969) have tabulated values of τ (barn/atom) for a wide energy range, supplied by J. H. Hubble of the N.B.S., Washington. I used the τ values for the atomic numbers 6, 7, 8, 13, 20 and 29 over the energy range 0.01 to 1.00 MeV, plotting τ as a function of Z on log-log paper. For each energy the plots could be well represented by a straight line; the gradients varied between 4.2 and 4.7, the average slope being 4.45. The exponent of Z in Walter's formula should therefore be 4.45, and that for Z and $\bar{Z}$ in Mayneord's expression 3.45, instead of 2.94. It is worth pointing out that in a recent review of attenuation coefficients, Hubble and Berger (1968) found that for the energy range $E = 10$ to 500 keV, and $Z = 1$ to 92, the product $\tau . E^3 Z^{-4.5}$, E being in MeV, was constant within reasonable limits.

The modified Mayneord formula, $\bar{Z}^{3.45} = \Sigma a_i Z_i^{3.45}$, is therefore recommended for calculating the effective $\bar{Z}$-values for photon and electron radiation. For water and mix D the values so derived are 7.50 and 7.52 respectively, in very good agreement.

The comedy of errors closes, as a comedy should, on a happy note, at any rate for mix D.

Yours, etc.
D. E. A. JONES.

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(*Received December, 1978.*)

REFERENCES

HIRAOKA, T., and KAWASHIMA, K., 1979. The atomic number of mix D. *British Journal of Radiology*, *52*, 330.

HUBBLE, J. H., and BERGER, M. J., 1968. Photon attenuation. *Engineering Compendium on Radiation Shielding*, *1*, (Springer-Verlag, Berlin).

JAYACHANDRAN, C. A., 1971. Calculated effective atomic number and kerma values for tissue-equivalent and dosimetry materials. *Physics in Medicine and Biology*, *16*, 617–623.

JOHNS, H. E., and CUNNINGHAM, J. R., 1969. *The Physics of Radiology*. 3rd edn., Appendix A, Tables A9–12 (Charles C. Thomas, Springfield, Il., U.S.A.).

JONES, D. E. A., and RAINE, H. C., 1949. Letter. *British Journal of Radiology*, *22*, 549–550.

MAYNEORD, W. V., 1937. The significance of the röntgen. *Acta of the International Union Against Cancer*, *2*, 271.

SPIERS, F. W., 1946. Effective atomic number and energy absorption in tissues. *British Journal of Radiology*, *19*, 52–63.

WALTER, B., 1929. *Fortschritte auf dem Gebiete der Röntgenstrahlen*, *35*, 929.

Wedged fields of the Philips treatment planning system

THE EDITOR—SIR,

In a recent article by Dale (1978) an evaluation of the accuracy of the Philips treatment planning system (TPS) teletherapy program was described. Although the general conclusion was favourable, Dale remarks "the TPS wedged isodose curves are not in quite the same agreement with our plotted curves as was found to be the case with non-wedged fields". We think our program deserves better than this, and feel that the judgement of wedged fields would have been more positive if isodose curves from the wedge section instead of the compensator section in the program had been used in the comparison.

The TPS employs an extended and improved version of the projective photon beam model described by Van de Geijn (1972). In his method compensators and wedges are taken into account by computation of the transmission of primary radiation by the filter and an elementary scatter distribution correction. In the TPS program the transmission of primary radiation is computed for actual path lengths even for shaped filters. Recently it has also been extended to rectangular and irregular beam shaping blocks.

Scatter distribution corrections related to the modified intensity distribution have evolved from the basic flattening and filter functions described by Van de Geijn (1972). These are dependent on the type of filter used. A compensator is used to compensate for oblique incidence in order to obtain isodoses which intersect the central axis approximately at right angles. The dose distribution shows little asymmetry and a symmetrical differential scatter correction (DSC) as for open beams is applied.

Wedges serve to incline the isodose curves on purpose. The intensity distribution is highly asymmetrical and this influences the scatter distribution. For this purpose an asymmetrical differential scatter correction (ADSC) is applied. This ADSC is dependent on spatial position in the field, field size and shape, wedge angle and photon energy. Isodose curves for wedged beams are renormalized to the position of maximum absorbed dose on the beam axis, as recommended by ICRU reports 10d (1963) and 24 (1976). For beam shaping blocks other scatter correction algorithms are employed.

Dale compared plotted wedged isodose curves with computed compensated isodose curves, *i.e.* without ADSC and so for obvious reasons finds "discrepancies which tend to increase with increasing field size and wedge angle". From extensive experiments we know that with the sophisticated ADSC inaccuracies are within 2% of peak dose even for large fields and steep wedges.

Yours etc.,
P. A. M. VAN OVERBEEK.

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(*Received November, 1978*)

REFERENCES

DALE, R. G., 1978. Implementation of the Philips treatment planning system for use in radiation teletherapy. *British Journal of Radiology*, *51*, 613–621.

VAN DE GEIJN, J., 1972. EXTDØS 71. Revised and expanded version of EXTDØS, a program for treatment planning in external beam therapy. *Computer Programs in Biomedicine*, *2*, 169–177.

ICRU Report 10d, 1963. *Clinical Dosimetry*.

ICRU Report 24, 1976. *Determination of Absorbed dose in a Patient Irradicated by Beams of X or gamma rays in Radiotherapy Procedures.*

Correspondence

(*In reply*)

Wedged fields of the Philips treatment planning system

The Editor—Sir,

With reference to Dr. Van Overbeek's letter (1979). Whilst accepting that it would be a fairer check on the beam accuracy to compare computed wedged curves with plotted wedged curves, it needs to be re-emphasised that in all our routine TPS planning the wedged fields have to be called from the computer as "compensators" in order to maintain the wedge normalization convention with which all the radiotherapy staff are familiar. In many hospitals it is common practice to express the wedge field isodose curves in terms of the equivalent unwedged field, but this cannot be achieved with isodose curves from the wedge section of the TPS without cross-reference to tables of wedge factors. This point was clearly made in the original paper (Dale, 1978), which presents the system accuracy as it is found when the said planning conventions are maintained.

Yours etc.,
R. G. Dale.

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REFERENCES

Dale, R. G., 1978. Implementation of the Philips treatment planning system for use in radiation teletherapy. *British Journal of Radiology*, *51*, 613–621.

Van Overbeek, P. A. M., 1979. Wedged fields of the Philips treatment planning system. *British Journal of Radiology*, *52*, 331.

The sensitivity of the human breast to cancer induction by ionizing radiation

The Editor—Sir,

In the review article by R. H. Mole (1978), the statement is made, "Since radiotherapy is part of the treatment for breast cancer and since the untreated breast is bound to receive some dose, the observations discussed above would lead to the prediction that subsequent frequency of breast cancer would be raised in the untreated breast and that this increase in frequency would be more conspicuous the younger the age at which treatment had been given. Both predictions appear to be supported by observations". He then quotes Brinkley and Haybittle (1968), Waterhouse and Prior (1975) and MacMahon *et al.* (1973).

Waterhouse and Prior relate the increased incidence of subsequent second primary tumours in the opposite breast and ovarian tumours in premenopausal patients with breast cancer. Their report did not relate these occurrences to irradiation treatment, nor is there any reference to the frequency of irradiation in these patients. I do not feel that this reference can reasonably be used as evidence to support Mole's hypothesis. In Brinkley and Haybittle's article, the patients analysed included both patients who received radiation therapy and those who did not. In that article, the authors did not imply or state that radiation was responsible for the increased incidence of breast cancer in the other breast.

If one reads MacMahon *et al.*'s article carefully, one notes that multiple bilateral primary breast cancer has been reported in a number of series with a frequency from seven to 15%. Urban (1969) has reported that women undergoing a random biopsy of the contralateral breast at the time of mastectomy had a bilaterality rate of 20%. Neither MacMahon's nor Urban's reports refer to patients who received any radiation or radiation therapy for breast cancer.

Therefore to imply, as Mole does, that radiation therapy for primary breast cancer might be associated with the development of secondary breast cancer in view of the evidence he presents and evidence cited is, in my opinion, unwarranted.

Yours, etc.,
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REFERENCES

Brinkley, D., and Haybittle, J. L., 1968. A 15-year follow-up study of patients treated for carcinoma of the breast. *British Journal of Radiology*, *41*, 215–221.

MacMahon, B., Cole, P., and Brown, J., 1973. Etiology of human breast cancer: a review. *Journal of the National Cancer Institute*, *50*, 21–42.

Mole, R. H., 1978. Review article. The sensitivity of the human breast to cancer induction by ionizing radiation. *British Journal of Radiology*, *51*, 401–405.

Urban, J. A., 1969. Bilateral breast cancer. *Cancer*, *24*, 1310–1313.

Waterhouse, J. A. H., and Prior, M. P., 1975. Breast cancer in young women. *British Medical Journal*, *3*, 434.

(*In reply*)

The sensitivity of the human breast to cancer induction by ionizing radiation

The Editor—Sir,

Dr. Levitt and I must have differed in our understanding of the word "appear" in my sentence "Both predictions appear to be supported by observations." After citing several I went on "However there is as yet no evidence to tell how much of these observed differences may be attributed to biological factors and how much, if any, to radiotherapy", intending to contrast appearance with evidence. Published articles on breast cancer which have not considered the possibility of induction by radiotherapy, like those cited by Dr. Levitt, cannot be regarded as bearing on that question. If the development of breast cancer in excess of the expected follows mutiple diagnostic exposures and radiotherapy of benign breast lesions, is it really unwarranted to raise the possibility that radiotherapy can do this also?

Yours, etc.,
R. H. Mole.

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(*Received January, 1979*)

Number of casualty attenders referred for X-ray examination

The Editor—Sir,

The excellent paper on the problems of X-ray wastage (Boulis *et al.*, 1978) restated a claim made in a leading article in the *British Medical Journal* (1977) that two thirds

TABLE I

CASUALTY ATTENDERS REFERRED FOR X-RAY EXAMINATION

Hospital	Type of hospital	Year	Full time Casualty Consultant in post	Number of first time attendees to casualty	Attenders X-rayed	
					Number	% of first time attenders
A	MT	1973	No	31 308	15365	49
		1976	Yes	30377	14199	47
B	MT	1973	No	19725	7896	40
		1976	Yes	23 298	10545	45
C	MT	1973	No	38097	22874	60
		1976	No	36267	24267	67
D	MT	1973	NA	NA	NA	NA
		1976	No	36390	13302	37
E	MT	1973	Yes	22000	14520	66
		1976	Yes	48000	31680	66
F	MT	1973	NA	NA	NA	NA
		1976	Yes	30205	13054	43
G	MT	1973	No	52660	19410	37
		1976	No	50426	23308	46
H	MD	1973	Yes	37946	13050	34
		1976	Yes	38111	14995	39
I	MD	1973	Yes	36650	15987	44
		1976	Yes	37605	15723	42
J	MD	1973	No	15856	6408	40
		1976	No	20237	7547	37
K	MD	1973	No	47154	14343	30
		1976	No	41805	13349	32
L	MD	1973	NA	NA	NA	NA
		1976	Yes	35754	17195	48
M	MD	1973	No	20510	7104	35
		1976	No	22159	7720	35
N	CD	1973	No	5006	2519	50
		1976	No	4511	2630	58
O	CD	1973	NA	NA	NA	NA
		1976	No	11076	4652	42
P	CD	1973	NA	NA	NA	NA
		1976	Yes	25074	12492	50
Q	CD	1973	No	17111	10312	60
		1976	Yes	20611	12645	61
R	CD	1973	Yes	25677	15580	61
		1976	Yes	25111	15053	60
S	CD	1973	No	30057	14250	47
		1976	No	31452	14178	45
T	CD	1973	NA	NA	NA	NA
		1976–7	Yes	19898	8086	41
U	CD	1973	No	36550	14976	41
		1976	No	37280	12438	33
V	CD	1973	Yes	42728	22635	53
		1976	Yes	41315	21992	53

MT = Metropolitan Teaching Hospital; MD = Metropolitan District Hospital; CD = Country District Hospital; NA = Not available.

1979, *British Journal of Radiology*, *52*, 334

of all new casualty attenders have an X-ray examination. The *British Medical Journal* leader had used figures from one hospital only. It is worth recording that the average number of casualty attenders referred for X-ray is in fact considerably less than 67%.

The radiology department of St. George's Hospital, London, recently completed a study of over 2000 casualty attenders (de Lacey, 1976; de Lacey *et al.*, 1978; de Lacey and Bradbrooke, 1978; de Lacey and Guilding, 1979). Subsequent to this study I sent a questionnaire to 62 hospitals in the United Kingdom and Eire. Many hospitals understandably had difficulty obtaining figures, but detailed replies were received from 22 X-ray departments (Table I). Most hospitals gave figures for first time attenders to casualty, and those who could only give the total number of attenders are only included in Table I if they stated that the additional numbers not attending for the first time was very small.

During 1973, 47% of first time attenders to casualty were referred for X-ray examination in these hospitals. In 1976, less than half of the attenders (47%) were again referred for X-rays. These figures probably err on the high side. This is because some hospitals could only give the total number of patients X-rayed in casualty, and this included some GP requests and/or emergency bed service admissions, and/or some fracture clinic patients. These additional patients will contribute to a falsely high reading as regards casualty attenders sent for X-ray.

This small survey includes figures from Metropolitan Teaching Hospitals (MT in Table I), Metropolitan District General Hospitals (MD) and Country District General Hospitals (CD). It is surprising that some casualty units X ray nearly 70% of attenders and others only 30%, though the reasons are not immediately obvious, nor is the effect on X-ray referral of a full-time Casualty Consultant. There are probably several explanations for the disparity, one of which could be blanket X-ray policies which may be in practice—*e.g.* an edict that all head injuries must have skull X-rays (Brindle, 1978)

Yours, etc.,
G. de Lacey.

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(*Received November, 1978*)

REFERENCES

Boulis, Z. F., Dick, R. and Barnes, N. R., 1978. Head injuries in children—aetiology, symptoms, physical findings and X-ray wastage. *British Journal of Radiology*, *51*, 851–854.

Brindle, M. J., 1978. Radiology work load—a solution. *British Medical Journal*, *2*, 514–515.

British Medical Journal, 1977. Clinical audit in diagnostic radiology. Leading article, *2*, 479.

de Lacey, G. J., 1976. Clinical and economic aspects of the use of X rays in the accident and emergency department. *Proceedings of the Royal Society of Medicine*, *69*, 758–759.

de Lacey, G. J., Wignall, B. K., Hussain, S. and Reidy, J. R., 1977. The radiology of nasal injuries: problems of interpretation and clinical relevance. *British Journal of Radiology*, *50*, 412–414.

de Lacey, G. J., Barker, A., Wignall, B. K., Reidy, J. R. and Harper, J., 1978. Analysis of reasons for requesting X-rays in the accident department (unpublished).

de Lacey, G. J. and Bradbrooke, S., 1978. Rationalizing requests for X-ray examination of acute ankle injuries (unpublished).

de Lacey, G. J. and Guilding, A., 1979. Mild head injuries: a source of excessive radiography? (in preparation).

Iconoscopy

The Editor—Sir,

Further proposal: That the international term "iconoscopy" should be used to include all activities associated with body-imaging.

C. B. A. J. Puijlaert in his interesting letter (Puijlaert, 1978) proposes the name "medical iconography" to include all "body-imaging" techniques. There is no doubt that any new name finally adopted must meet the criteria he enumerates and initially "medical iconography" sounds a good candidate. However, are not the objections Dr. Puijlaert formulates in his second paragraph too important to be ignored? All the more so since "iconography" does not only mean the description of paintings, but also the illustration of a subject by pictures, and in a much broader sense, the assembling and listing of all the iconic documents associated with a subject or person. As such it could already be associated with medicine (the iconography of 17th century medicine for instance might well include engravings of contemporary surgeons or hospitals as well as anatomical engravings of the time) and this could cause confusion.

The same applies also to "iconology" (para. 7), the description, history or analysis of artistic symbolism, often associated with the theories of Erwin Panofsky (Panofsky, 1972). There again the term might well be applied to aspects of medicine and lead to confusion (it might for instance be used to mean the elucidation of symbols like Aesculapius' snake etc.). Since there is a case for using the same root both for the name of the science and that of its practitioners, could not "iconoscopy" (and "iconoscopist") be used instead, since all those who use body-imaging techniques use them not so much by making them as by looking at them with an eye trained by knowledge and experience? These words have not yet been used and could be not associated with any other discipline or practice. Neither "medical" nor "diagnostic" should be necessary. The word "iconoscope" exists, and refers to the oldest electronic analysing device for converting the optical image in the television camera into a sequence of electrical signals, and this is now obsolete. The suffix "scopy" could easily be applied to all the other roots indicated by Dr. Puijlaert in para. 8 except that, in order to avoid confusion, the old term "radiology" would doubtless still be used instead of "radioscopy". The distinction between radiologist and radiographer could be preserved as "iconoscopist" and "iconographer", since the latter word in one of its present senses—"a maker or designer of figures or drawings, especially of a conventional or mechanical type" (Webster, 1961)— corresponds to the technical expert's activity.

Yours, etc.,
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A. Lavers.

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REFERENCES

Panofsky, E., 1972 *Studies in iconology: humanistic themes in the art of the Renaissance* (Harper and Row, New York).

Puijlaert, C. B. A. J., 1978. Medical iconography. *British Journal of Radiology*, *51*, 930.

Webster, 1961. *Third New International Dictionary of the English Language* (G. Bell and Sons Ltd., London).

Correspondence

Photographic effect of varnish

THE EDITOR—SIR,

It is well understood that X-ray film must be stored with care, and in particular, any film container must be light tight and placed out of the way of penetrating radiations. What may not be as well known is the hazard of producing serious film fogging from exposure of the emulsion to surfaces that are apparently photographically inert. We would like to publicize a powerful fogging action which we have recently encountered, arising from ordinary polyurethane varnish used to seal and stain the inner wooden surfaces of a film hopper. Films left against the inside of a newly constructed hopper treated with a single coat of matt polyurethane varnish (Ronseal) for 24 hours showed an overall average density of 0.8 upon development. Even some weeks after the application of the varnish, it still produced a serious fog with conventional rapid process film. All other sources of the fogging (such as the wood itself, light leaks, X-ray penetration, or even of turpentine in the paint brushes used) have been eliminated by controlled experiments. Of some particular interest is the pattern of the fogging. For thick coats, the radiograph will show the individual brush strokes, while thin coats give a faithful (and rather attractive) reproduction of the wood grain, presumably because of the differential absorption of the varnish.

Apparently similar such effects have been reported before, and they are often attributed to the action on the film of reducing agents, such as hydrogen peroxide, produced when paints harden. However, we feel that many X-ray departments will not be sufficiently aware of the trouble that may be caused by such a commonly used material, and may be grateful for being forewarned.

Yours, etc.,
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J. C. GORE,
G. HOOKER.

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(*Received November, 1978*)

Digital electronic watches and X-ray examinations

THE EDITOR—SIR,

Recently, two patients undergoing X-ray examinations at Whiston Hospital complained that their digital watches had stopped at the time of the examination. It then emerged that a medical physics technician had independently noted that his digital watch had apparently been affected following the performance of radiation safety surveys in diagnostic X-ray departments and the watch is no longer capable of correct operation.

To investigate this problem, two digital watches were subjected to a wide range of radiation exposures from a diagnostic X-ray machine but no observable detrimental effect occurred. We also wrote to the company marketing the watches and received the following reply.

"Watches of the type mentioned by you use CMOS chips, which can be affected by radiation; in some cases they recover. There is still somewhat of a grey area in CMOS technology and it is suggested that watches should not be worn in an area of high radiation. The product may be damaged in the presence of a magnetic field and you may know whether this applies to X-ray equipment."

These events may have been fortuitous but we should be interested to learn of any similar episodes. In the meantime, it may be prudent to ask patients with digital watches to remove these prior to X-ray examinations and to place the watches well away from the X-ray generator.

Yours, etc.,
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E. T. HENSHAW.

Radiological Protection Adviser,
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(*Received December, 1978*)

Book review

Radiology Study Guide. By K. Simpkins, pp. 215, illus. (University of Leeds). £5·50 UK; £6·50 overseas.

An interesting transformation takes place in candidates sitting the F.R.C.R. examination. Before the event most candidates regard it with trepidation as a formidable hurdle. After the examination one of two attitudes develops. Those who have failed are confirmed in their view that the examination is unduly difficult; that the examiners are somewhat less than fair and that the College authorities have manipulated the pass rate in order to keep passes down. Successful candidates, on the other hand, suddenly realize that the examination is fair and that there would be no point in having a fellowship if the standards are not kept high.

Examiners are constantly heard to say that candidates fail themselves, since many do not know how to prepare for the battle. This is where Dr. Simpkins' book will prove its value. Those already familiar with his writings will know what to expect (the others, incidentally, should proceed to their library forthwith and repair the defect). The book has all the wit and good sense one could hope for, and is nicely spiced with amusing illustrations.

It falls into two parts. The first part consists of general advice on how to prepare for and how to behave during the examination. Notwithstanding the occasional dig at the examiners, this is all good stuff and should be taken to heart by candidates.

The second part is perhaps even more valuable. It consists of a list of suggested reading. This has been very carefully selected, and the great thing about it is that it is realistic. It should be quite possible for any candidate to cope with the material in the three years available to him. If he has read and retained it he should have very little difficulty in passing the F.R.C.R.—provided, also, that he has enough practical experience at film interpretation.

The book is to be thoroughly recommended to candidates, and Dr. Simpkins should be congratulated on his enterprise in having written it.

F. STARER.

1979, *British Journal of Radiology*, *52*, 336–350

Proceedings of The British Institute of Radiology

Thirty-sixth Annual Congress and Joint Meeting (April 13–14, 1978)

Abstracts of papers read at The British Institute of Radiology Thirty-sixth Annual Congress and Joint Meeting with the Netherlands Society of Diagnostic Radiology, Netherlands Society of Therapeutic Radiology, Royal College of Radiologists and Royal Society of Medicine (Section of Radiology) held at the R.I.B.A. 66 Portland Place, London W1 on April 13–14, 1978

Assessing pelvic tumours

Chairman: Dr. R. Morrison
Diagnostic ultrasound, by Patricia Morley.
Lymphography, by J. S. Macdonald.
Computed tomography in pelvic tumours, by Janet E. Husband.
Lymphoscintigraphy of the pelvis, by M. V. Merrick and A. E. Kirkpatrick.
Comparison between ultrasound and computer tomography in the pelvis, by D. H. W. Schönfeld and P. F. G. M. van Waes.

DIAGNOSTIC ULTRASOUND

By Patricia Morley

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Western Infirmary, Glasgow G11 6NT

Ultrasonic assessment of pelvic pathology depends upon accurate reproduction of cross sectional detail combined with analysis of the morphology and acoustic properties of identified mass lesions. High frequency transducers and carefully selected sensitivity are employed to demonstrate soft tissue detail. For complete assessment, examination of the renal tract, liver, abdominal nodes and peritoneal cavity may be necessary.

Ultrasound has for years been established as the procedure of choice in differentiating cystic and solid mass lesions. This information is frequently used only to confirm a clinical diagnosis prior to laparotomy and may therefore not alter management of the patient significantly. In a large series of histologically confirmed ovarian tumours ultrasound was only marginally better at confidently diagnosing ovarian malignancy than a competent clinical examination. A more detailed analysis demonstrated that the ultrasonic scan identified signs associated with malignancy in a higher proportion of stage I and stage II tumours than did the clinical examination, though with stage III tumours there was no significant difference. However, attempts at pre-laparotomy clinical staging of these tumours by ultrasound was too inaccurate to be of clinical value and a significant proportion of a series of histologically benign tumours had echographic features which could be associated with malignancy. Though limited in the diagnosis and clinical staging of ovarian malignancy, serial scanning can detect recurrence or extension of the disease before it is clinically evident and post laparotomy ultrasonic monitoring is advocated.

Similar problems were encountered in the diagnosis and attempted staging of invasive endometrial carcinoma and a small group of leiomyosarcoma. However serial scanning after treatment accurately demonstrated local recurrence. Patients with carcinoma of the cervix were examined. Ultrasonic changes in the pelvic soft tissues could be defined in stage IIB, IIIB and IV. Scans after diagnosis may be of value in pretreatment clinical staging, the examination being-complementary to other conventional methods. Experience with a small number followed up after treatment showed that recurrence could be defined and suggested that radiation fibrosis and recurrent tumour may have different acoustic properties.

Over 300 patients with epithelial bladder tumours have been examined. Ultrasonic clinical staging was found to be accurate with the more invasive tumours and compared well with most radiographic methods of staging. However, differentiation of deep muscle invasion from early extension through the serosal coat was unreliable, and a confident diagnosis of involvement of other pelvic viscera could rarely be made. Conventional methods of clinical staging are accurate with superficial tumours but are poor when assessing invasive tumours; the converse applies to the ultrasonic examination and ultrasound is indicated as a complementary method of clinically staging bladder tumours and in monitoring invasive tumours during and after treatment.

Though it is now possible to obtain significantly useful information which can be used in diagnosis and, more effectively, in management after diagnosis, there are still limitations imposed by restricted sensitivity and inadequate resolution. There is also a lack of information on the acoustic properties of tissues in differing pathological processes and there is no established method of measuring these changes *in vivo*. If these limitations can be overcome ultrasound will become an even more significant diagnostic investigation.

LYMPHOGRAPHY

By J. S. Macdonald

Department of Diagnostic Radiology, The Royal Marsden Hospital, Downs Road, Sutton, Surrey

The lymphatic system is an important avenue of tumour spread and the elaboration of lymphography has contributed to the understanding and control of certain tumours. The more orderly the spread of the tumour, the more valuable the contribution of lymphography. The oily contrast medium remains in the nodes for long periods; this valuable asset should be used, and the concept of lymphography as a dynamic investigation is important.

Lymphography is a direct investigation and within its limits shows the nodes and the storage pattern of the contrast medium within them giving helpful information about possible pathology and whether a node is enlarged due to secondary deposit, lymphoma or reactive change.

Lymphography has the advantage that once the nodes are opacified their behaviour can be rapidly assessed by the use of a plain radiograph and the progress or extension of disease can be monitored. Spread out of the pelvis to the para-oartic nodes can radically alter the treatment.

If lymphography is omitted then an incomplete picture will be seen in 27% stage I carcinoma of the cervix, 20% carcinoma of the body of uterus, 23% carcinoma of the ovary, 30% of T_1 and T_2 carcinoma of the prostate and 23% of T_2 carcinoma of the bladder.

COMPUTED TOMOGRAPHY IN PELVIC TUMOURS

By Janet E. Husband

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We are investigating the value of computed tomography (CT) in pelvic malignant disease since these tumours can present problems not only in initial clinical staging but also in defining the effect of treatment and in the detection and assessment of recurrence.

One hundred and sixty-one scans have been performed in 122 patients with carcinoma of the cervix, uterus, ovary, rectum and bladder. Normal CT findings in these tumours are described and difficulties encountered both in technique and interpretation discussed. The CT findings in 25 patients with carcinoma of the bladder have been compared to the initial clinical stage. The results indicate that there is good correlation in 80% of patients but in addition CT gives valuable information in detecting the presence and extent of extra-vesical spread. We have used CT in an attempt to identify enlarged lymph nodes in the pelvis. Lymphograms were performed before the CT scan in 23 patients and the findings were compared. The results have been disappointing since only one out of seven patients with a positive lymphogram showed extra evidence of nodal disease with CT.

In 11 patients CT scans were performed after radiotherapy to monitor the effects of treatment. More than half the patients showed good tumour regression, whereas the remainder showed poor regression.

From this small series it may be concluded that CT is likely to be a valuable technique in the management of bladder tumours, particularly in demonstrating extra-vesical disease and in defining response to treatment.

LYMPHOSCINTIGRAPHY OF THE PELVIS

By M. V. Merrick and A. E. Kirkpatrick

University of Edinburgh, Department of Medical Radiology Western General Hospital and Royal Infirmary

Five techniques have been proposed as means of visualizing malignant involvement of lymph nodes of the pelvis.

1. The intravenous administration of so-called tumour localizing agents such as ^{67}Ga salts. There is ample evidence that these agents are even less reliable in the pelvis than they are in other sites, partly because of confusion with excreted activity remaining in the bowel, and partly because of unreliable and poor concentration of these agents within the tumour.
2. The intralymphatic administration of ^{67}Ga salts by bipedal lymphography. This has been performed in 27 patients undergoing lymphangiography, the injection of ^{67}Ga immediately preceding that of lipiodol. In no case was tumour in pelvic or para-aortic lymph nodes visualized by this technique.
3. The intralymphatic injection of ^{99}Tc^{m} albumin. Initial reports (Steckel *et al.*, 1978) suggest that observation of flow rates and flow patterns may be of value. This technique is as time-consuming as lymphangiography, but avoids the potential embolic hazards of iodinated oils. It may therefore be of use as a screening procedure in patients at particular risk from conventional lymphography. Additional experience is necessary to confirm this.
4. Intralymphatic injection of colloids. It has been suggested that disturbances of lymph-node function may occur early in malignant involvement, and possibly before deposits are large enough to be visualized by contrast lymphangiography. The evidence to support this hypothesis is meagre, and the lack of an ideal colloid preparation is a further complication.
5. Indirect radionuclide lymphangiography. Subcutaneously administered colloid is cleared to regional lymph nodes. ^{198}Au has been widely used (Zum Winkel and Scheer, 1965) despite its unfavourable radiation characteristics. Technetium labelled colloids are of larger particle size than gold colloid, and in consequence less passes beyond the most proximal lymph node group. Visualization of the more important distal nodes is therefore not as good. The technique has never achieved widespread acceptance.

The role of radioisotope techniques of investigation of the pelvis is therefore at present limited. There is a substantial need for better radiopharmaceuticals.

REFERENCES

STECKEL, R. J., FIRMANSKI, S., COLLINS, J. D. and POE, N., 1978. Clinical radionuclide perfusion lymphangiography. *British Journal of Radiology, 51,* 35–40.

ZUM WINKEL, K. and SCHEER, K. E., 1965. Scintigraphic and dynamic studies of the lymphatic system with radiocolloids. *Minerva Nucleare, 9,* 390–398.

COMPARISON BETWEEN ULTRASOUND AND COMPUTER TOMOGRAPHY IN THE PELVIS

D. H. W. Schönfeld and P. F. G. M. van Waes

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In our department we have been using CT scanners since mid-1977. Most patients examined for disease of the pelvis were also evaluated by means of ultrasound. In this relatively short time we have evaluated over 80 patients with suspected pelvic pathology with both modalities. Even though the number of patients is not great enough to enable us to do any statistical evaluation we do feel we can express some preliminary opinions.

Bladder: in the case of bladder pathology both modalities have their merits. Ultrasound is quite capable of finding bladder carcinoma and gives additional information on staging. A 3.5 mHz transducer has to be used. CT scanning is however more efficient in delineating extension into the various structures.

Uterus: in this area ultrasound is very well able to demonstrate pathology. In our experience CT scanning rarely adds any additional information.

Prostate: both modalities are able to show the volume of the organ. Ultrasound has the benefit that it can differentiate between carcinoma and prostatitis.

Ovary: recently W. F. Sample has shown that by means of ultrasound it is possible to depict the normal ovary and assess any possible pathology. We have not been able to show normal ovaries on the CT scanner. In the case of ovarian tumours both modalities showed any ascites which might be present and both showed the size of the tumour, but only CT scanning was able to image its complete extent and any soft-tissue involvement.

Lymph nodes: in deciding whether or not nodes are enlarged, we found CT scanning to be far superior to ultrasound in the pelvis. In order to evaluate them correctly we consider it necessary to have a lymphangiogram done prior to the CT scan. In addition thorough filling of all the intestine with gastrografin is essential in order to be able to delineate the lymph nodes. In most cases ultrasound was unable to do so because of bowel gas. At present we consider the use of lymphangiography and CT scanning the most worthwhile combination when looking for lymph node metastases in the pelvis. CT is essentially worth while when huge lymph nodes or even whole chains have not been filled with contrast in lymphangiography.

Soft tissue: the CT scan was found to be better in evaluating the extent of masses originating from such soft tissues as the intestine and muscle. Ultrasound can image these masses in many cases but does not show up neighbouring tissue involvement as well as CT. It did however sometimes demonstrate the exact nature of the mass, such as an abscess or a solid tumour.

In conclusion, we found the combined use of ultrasound and CT to be most beneficial in the evaluation of pelvic disease. When considering pelvic metastases to lymph nodes CT was especially valuable when combined with lymphangiography.

Radiology of head and chest injuries

Chairman: Dr. D. G. C. Whyte

Skull X-rays and CT scanning soon after head injury, by B. Jennett.
Angiography in head trauma, by H. O. M. Thyssen.
Nuclear medicine techniques in the investigation of trauma of the head and thorax, by M. N. Maisey.
Aspects of cavernous sinus fistulas, by F. Peeters.
Computed tomography of closed head injuries, by E. H. Burrows.

SKULL X-RAYS AND CT SCANNING SOON AFTER HEAD INJURY

By B. Jennett

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Detection of skull fracture after recent head injury is an essential component of assessment, particularly when the patient in casualty is fully conscious. In such patients a linear fracture increases the probability of an intracranial haematoma by about 400 times; in the comatose patient a fracture increases the risk by 20 times. Over 75% of patients with intracranial haematoma have a fracture (90% of adults with extradural haematomas). All patients who develop intracranial infection after recent trauma have a skull fracture. Failure to recognize compound depressed fracture if the vault or an open fracture of the base results in a much higher infection rate in civilian Britain than in American military hospitals in the Far East. Competent skull radiography in accident departments could reduce the number of admissions following mild head injury in Britian by 100,000 a year; good equipment, well instructed radiographers and casualty clinicians adequately trained to interpret the films are essential.

CT (EMI) scanning reliably detects intracranial haematoma, which is life-threatening and remediable. Mortality and morbidity remains high due to the delayed recognition of this complication, and this could be considerably reduced if more patients could be scanned during the first 24 hours after injury. Whole body scanners in general hospitals would be adequate for this purpose; moving of head injury patients to the nearest scanner is a strategy which must be considered in view of the scarcity of scanners.

ANGIOGRAPHY IN HEAD TRAUMA

By H. O. M. Thyssen

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Recognition of extracerebral haematomas is essential since operative evacuation is generally necessary. The angiographic diagnosis of the acute subdural or epidural haematoma, which show a rind-shaped or biconvex avascular space is well known.

However, in cases of a fronto-lateral or a temporo-occipital epidural haematoma such an avascular space is not always visible in the standard angiographic projections; special oblique projections may be necessary.

A problem in angiographic diagnosis is the subtemporal epidural haematoma which cannot be seen as an avascular space because of its location. It causes elevation of the trunk of the middle cerebral artery and has for this reason to be differentiated from an intracerebral temporal contusion or haematoma.

This differentiation depends on two criteria. The first uses the configuration of the vascular tree of the middle cerebral artery, the second, the course of the anterior ramus of the middle meningeal artery. The first series of criteria were developed from a model that describes the trunk of the middle cerebral artery, the insular and temporal cortical arteries as transverse meridians around the avoid body of the temporal lobe.

The use of this model in angiographic interpretation and comparison with operative findings disclosed that a gyrate course of the elevated trunk of the middle cerebral artery, its insular and opercular branches proved to be typical of intracerebral temporal contusion or haematoma. A rectilinear course of the trunk of this artery in conjunction with pseudo-elongation by insular branches was typical of the subtemporal epidural haematoma.

The second group of criteria emerges from the location of the dura mater at the skull-base of the middle cranial fossa. Dislocation of it by a subtemporal epidural haematoma can be diagnosed by the abnormal course of the anterior branch of the middle meningeal artery. The optimal angiographic projections, variations and aberrations in its course are demonstrated. Correct interpretation of its course provides further evidence for differentiating an intracerebral temporal haematoma or contusion from a subtemporal epidural haematoma.

NUCLEAR MEDICINE TECHNIQUES ON THE INVESTIGATION OF TRAUMA OF THE HEAD AND THORAX

By M. N. Maisey

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The accuracy of brain scanning in the diagnosis of subdural haematoma is 85–90% in different series. This increases to an accuracy of up to 95% when static brain imaging is combined with dynamic perfusion studies, especially in children. Nuclear medicine investigations play a small part in the investigation of selected patients with extradural haematomata, cerebral contusion and traumatic CSF rhinorrhoea. Lesions simulating subdural haematomata include skull and scalp disease, epidural collections, meningitis, cerebral contusion and peripheral metastases. Radionuclide studies of the chest following trauma include bone scans for spinal and rib injury, perfusion and ventilation lung scans for blunt non-penetrating trauma and inhalation trauma, thallium^{201} myocardial perfusion scans and ^{99}Tc^{m} labelled red blood cell MUGA following cardiac trauma. Trauma to the liver and spleen is frequently associated with thoracic trauma and can be detected using the routine ^{99}Tc^{m} sulphur colloid liver/spleen scan with a low incidence of false negative results. Nuclear medicine with its advantages of simplicity, low morbidity and the introduction of mobile gamma cameras has an important part in the investigation of trauma.

ASPECTS OF CAVERNOUS SINUS FISTULAS

By F. Peeters

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There are three types of carotid-cavernous fistula:

1. Dural internal carotid cavernous sinus fistula: communication between meningeal branches of the internal carotid artery and the cavernous sinus;
2. Dural external carotid cavernous sinus fistula: communication between meningeal branches of the external carotid artery and the cavernous sinus;
3. Direct internal carotid cavernous sinus fistula: direct communication between the intracavernous part of internal carotid artery and the cavernous sinus.

Fistulae of the dural type often develop spontaneously. The flow through the fistula is slow, the clinical symptoms are mild, and spontaneous closure is not rare.

Direct fistulae develop post-traumatically or due to rupture of an aneurysm. The flow through the fistula is rapid and the clinical symptoms (exophthalmos and oculomotor paralysis) are severe.

Embolization after selective catheterization is the method of choice in the treatment of dural fistulae from the external carotid artery. In the treatment of dural fistulae from the internal carotid artery, occlusion of the internal carotid artery in the area of the meningeal vessels by means of a small balloon is a promising procedure.

Today, direct fistulae between the internal carotid artery and the cavernous sinus can be closed with the aid of a balloon in the cavernous sinus; this technique, known as the inflatable and released balloon technique, has the important advantage that the internal carotid artery remains patent.

The roentgenographic and therapeutic features of the various types of cavernous sinus fistula are discussed with reference to a series of 18 patients.

COMPUTED TOMOGRAPHY OF CLOSED HEAD INJURIES

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Computed tomography of the brain is the primary investigation of choice in acute head injuries, because it tells the surgeon whether operative intervention will benefit or harm the patient. The diagnostic picture of the intracranial compartment provided is unequalled by any other investigation that can be performed in life, and is surpassed in the yield of clinical information only by post-mortem brain cutting. Skull radiography and carotid angiography are of lesser value and, if carried out subsequently, seldom provide any further useful information (Merino-de Villasante and Taveras, 1963). Extracerebral collections can be easily distinguished from haemorrhagic cerebral contusions, and post traumatic sequelae and damage accurately monitored.

Diagnostically difficult problems that are made easier by CT scanning are: (1) Extracerebral collections that are complicated by cerebral contusions which adversely affect the prognosis: such contusions may not be detectable by other radiological means. (2) Posterior fossa haematomas. (3) The extent of extracerebral collections, including their bilaterality (Ambrose and Gooding, 1976).

Subacute extracerebral collections become isodense with the parenchyma of the brain after several weeks, and diagnosis depends on demonstrating the typical ventricular deformity and midline displacement; the actual lesion may not be outlined (Svendsen, 1976).

REFERENCES

AMBROSE, J. and GOODING, M. R., 1976. EMI scan in the management of head injuries. *The Lancet*, April 17, 1976, 847–848.

MERINO-DE VILLASANTE, M. D. and TAVERAS, J. M., 1976. Computerized tomography (CT) in acute head trauma. *American Journal of Roentgenology*, *126*, 765–778.

SVENDSEN, P., 1976. Computer tomography of traumatic extracerebral lesions. *British Journal of Radiology*, *49*, 1004–1012.

Growing points in human tumour radiobiology

Chairman: Prof. K. Breur

A radiobiological assessment of cervical carcinoma, by B. Dixon.
Tolerance of normal tissues in patients. Comparison of different models, by C. F. Westermann and G. Kok.
Human tumour xenografts for studies in experimental chemotherapy and radiotherapy, by G. G. Steel.
Fractionated irradiation of a human malignant melanoma grown in athymic nude mice in the presence and absence of the hypoxic cell radiosensitizer misonidazole, by E. K. Rofstad and T. Brustad.
Measurement of the reponse of primary carcinoma of the breast to treatment, by R. H. Thomlinson.
Responses of different experimental tumours to irradiation in relation to their cellular radiosensitivity *in vitro*, by G. W. Barendsen.

A RADIOBIOLOGICAL ASSESSMENT OF CERVICAL CARCINOMA

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Radiobiology may take two pathways in developing its role in improving the treatment of cancer by irradiation. The first is taken by many experimentalists using their laboratory animal models to devise and evaluate the potential of new treatment methods. The second pathway, still yet largely unexplored, is to examine more closely patients and their tumours as they present themselves daily to the radiotherapist. With cervical cancer the latter approach requires of the radiobiologist a clear definition of the clinical problem and an acceptance of the limitations of working with tumour biopsies. Two laboratory techniques may be used to study cervical tumours and their response to radical radiotherapy: tritiated thymidine (^{3}H-TdR) autoradiography and Feulgen DNA microdensitometry.

In vitro ^{3}H-TdR studies of biopsies from 54 patients (Dixon *et al.*, 1977) have shown that the proliferative activity of the vaginal component of the tumour varies and the labelling index ranges from 2 to 30%. With advancing clinical stage the potential doubling time of cycling cells increases from one day (stages I + II) to eight days (stage III + IV). During radiotherapy with ^{60}Co cathetron insertions and external pelvic irradiation, the tumour response is related to pre-treatment labelling, as is the time taken to resolve the vaginal component of tumour subsequent to treatment. The proliferative activity of the tumour does not appear to be related however to long term prognosis, *i.e.* the probability of developing recurrent or metastatic disease.

A complementary study of tumour biopsies of 125 patients by Feulgen microdensitometry (Dixon and Stead, 1977) has shown that by computer analysis of data, cellular kinetic information may also be obtained for about 70% of patients with near diploid (2C) or tetraploid (4C) tumours. Other patients have either 2C–4C tumours (15%) or aneuploid tumours (15%). Though "ploidy" is independent of clinical stage, changes in the DNA content of tumour cells as radiotherapy progresses may in quantitative terms be used to monitor its effect. In 70 patients followed for two years, those with 2C tumours fared worse, only 45% being tumour-free compared with 63% with aneuploid or 4C tumours.

REFERENCES

Dixon, B., Ward, A. J. and Joslin, C. A. F., 1977. Pretreatment ^{3}H-TdR labelling of cervical biopsies: histology, staging and tumour response to radiotherapy. *Clinical Radiology*, *28*, 491–497.

Dixon, B. and Stead, R., 1977. Feulgen microdensitometry and analysis of S-phase cells in cervical tumour biopsies. *Journal of Clinical Pathology*, *30*, 907–913.

TOLERANCE OF NORMAL TISSUES IN PATIENTS. COMPARISON OF DIFFERENT MODELS

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On theoretical grounds it can be expected that the exponents $\alpha=0.24$ and $\beta=0.11$ in Ellis' NSD formula should be dependent on radiobiological parameters. Experimentally it is found that α and β can have different values (Wara *et al.*, 1973; Van der Kogel and Barendsen, 1974; and Wollin and Kagan, 1976).

We performed a retrospective investigation of two groups of patients:

1. A group of 70 patients with carcinoma of the larynx. Tissue tolerance was estimated by percentage of incidence and severity of late oedema. Best correlation was found with Wollin and with a modified NSD ($\alpha=0.31$, $\beta=0.11$). The tumour effect however did not show a relation with these NSD-type parameters, but tumour response was correlated with total treatment time, the effect being better as this time was shorter.

2. A group of 40 patients with inoperable mammary carcinoma. Here incidence and severity of induration were scored. A volume correction factor was applied of 4% in dose per factor of 2 in treated volume. The best correlation was found with Wara's ED; NSD was nearly as good. A difference of 10% in dose, NSD or ED produced in both groups a significant difference in tissue reaction.

With the aid of good three-dimensional computer-planning and a uniform characterization of tissue damage it appears to be possible to acquire fairly accurate radiobiological results from clinical data.

REFERENCES

Van der Kogel, A. J. and Barendsen, G. W. 1974. Late effects of spinal cord irradiation with 300 kV X-rays and 15 MeV neutrons. *British Journal of Radiology*, *47*, 393–398.

Wara, W. M., Phillips, T. L., Margolis, L. W. Smith, V., 1973. Radiation pneumonitis: a new approach to the derivation of time-dose factors. *Cancer*, *33*, 547–554.

Wollin, M. and Kagan, A. R., 1976. Modification of the biologic dose to normal tissue by daily fraction. *Acta Radiologica*, *15*, 481–492.

HUMAN TUMOUR XENOGRAFTS FOR STUDIES IN EXPERIMENTAL CHEMOTHERAPY AND RADIOTHERAPY

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Human tumours transplanted into immune-deficient mice provide a new type of tumour material that is being explored for experimental studies in radiotherapy and chemotherapy. There is now a substantial body of data on take-rates that shows that colonic carcinomas, melanomas and oat-cell carcinomas are examples of tumour types that give relatively high take-rates. Certain other tumours, especially sarcomas and carcinoma of the breast, transplant poorly. Various laboratory animals have been used for grafting; in recent years the main emphasis has been upon the use of congentitally athymic (nude) mice or mice immune-suppressed by lethal whole-body irradiation with bone marrow reconstitution or protection. Xenografted tumours often maintain the histological characteristics of the parent tumour. They have also been shown in certain cases to maintain hormone-dependence and the production of marker proteins. Metastasis is not frequently observed but has been found in a few studies with xenografted tumours.

Therapeutic response has been estimated either by the *in situ* measurement of tumour growth delay or by clonogenic assays. The growth delay work has shown that in some cases xenografts respond to chemotherapeutic agents in a way that is consistent with the ranking of these agents in clinical use. The attempt to compare directly the clinical response of a patient with his own xenografts has not proceeded far but the available results are encouraging.

Cell cloning of xenografted human tumours has been performed both *in vitro* in soft agar and in agar diffusion chambers. The cell survival curves that these studies have produced have allowed cellular sensitivity to be accurately documented and have revealed a wide range of sensitivity of a particular tumour to a range of drugs and of various tumours to certain selected drugs.

The main disadvantages of xenografts are the changes, kinetic and otherwise, that the tumours undergo on transplantation; the fact that the tumours consist of human cells supported by a mouse stroma; and the likelihood that xenografts probably grow in the face of a substantial host resistance against them. The impact of these drawbacks on experimental therapeutic studies has yet to be fully explored and work in this area should therefore be pursued cautiously.

FRACTIONATED IRRADIATION OF A HUMAN MALIGNANT MELANOMA GROWN IN ATHYMIC NUDE MICE IN THE PRESENCE AND ABSENCE OF THE HYPOXIC CELL RADIOSENSITIZER MISONIDAZOLE

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A study has been conducted on the effect of the hypoxic cell radiosensitizer misonidazole (Ro-07-0582) (gift from Roche Chemical Co. Ltd., England) during fractionated irradiation of a human malignant melanoma grown subcutaneously in the athymic mutant nude mouse. Misonidazole in doses of 500 mg/kg bodyweight was administered to the animals by intraperitoneal injection 45 min before each exposure to ^{60}Co γ rays. For a single dose of 12.50 Gy, the enhancement ratio of misonidazole was found to be 1.5. For three fractions, each of 4.52 Gy, it was found to be 1.15. For four fractions, each of 3.75 Gy; it was found to be 1.05 and for 10 fractions, each of 2.07 Gy, no sensitization was observed at all. The fractions were all given at 24 hour intervals, and the enhancement ratio for each fractionation regime was determined by comparing the tumour regrowth delay with that observed after similar fractionated treatments without radiosensitizer. The present study indicates that this human melanoma, when grown in the mutant nude mouse, contains hypoxic cells and that the tumour reoxigenates quite efficiently during the first day after being exposed to a relatively small dose of γ rays. In order to obtain a clinical benefit of misonidazole for the malignant melanoma studied, the present results suggest that the drug must be used in combination with fractionation regimes based on few fractions and relatively large doses per fraction.

MEASUREMENT OF THE RESPONSE OF PRIMARY CARCINOMA OF THE BREAST TO TREATMENT

By R. H. Thomlinson

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The changing size of primary carcinoma of the breast has been determined in 60 patients and the data presented are based on almost 11,000 measurements of diameter made by a pair of observers. The tumours have been treated with radiotherapy, cytotoxic drugs or hormones.

The following conclusions may be drawn:

1. All tumours have responded to treatment as shown by inhibition of growth and some degree of regression.
2. Curves relating tumour volume to time during the period of regression are all exponential, *irrespective* of the size or type of tumour and the treatment given. The average value of the coefficient of correlation between the observations of size and time, derived from 74 regression curves, is 0.95.
3. There is a 38 fold range in the slopes of the regression curves of tumours in different patients receiving essentially the same treatment.
4. It is possible, from the data, to discriminate with 95% confidence slopes that differ by a factor of 1.5.
5. From ten pairs of slopes from patients who have been treated sequentially with cytotoxic drugs and radiotherapy, the slopes of the regression curves for the same patient receiving different treatments are indistinguishable at the 95% confidence level.
6. There is no correlation between the initial size of the tumour and the slope of the regression curve.
7. Toward the extremes of the range of the regression slopes there is an obvious relationship between the steepness and the histological structures of the tumour.
8. Tumours that re-grow after therapy grow exponentially.
9. Measurement is sufficiently accurate to establish growth rates from an increase in diameter of less than 20 mm.
10. The range of slopes of regrowth is about as wide as that of regression.
11. There is probably a good correlation between the rate of regression and the rate of regrowth after chemotherapy but not so good after radiotherapy. On the whole tumours grow relatively more slowly after radiotherapy than after chemotherapy.

These data imply that the changing size of primary carcinomas of the breast in response to treatment may be represented by a letter "V", the two arms of which correspond to slopes of regression and regrowth curves intersecting at a point related to minimum size. These parameters are characteristics of the tumour not of the treatments being given. These data are also consistent with data previously obtained from multiple metastases in individual patients and transplanted tumours in rats.

If the principles are generally true, there are certain implications for all clinical trials. In any event they apply to clinical trials of carcinoma of the breast. The rate of regression and therefore the degree of regression of a tumour in a given time is no measure of the effectiveness of treatment, and should be abandoned as a criterion. The same statement is true for the minimum size.

The delay imposed on growth may be an indication of the effectiveness of treatment in terms of its killing clonogenic cells, but only if expressed in terms of the growth rate of each tumour.

The pattern of response, being an inherent quality of each tumour, forms a basis for characterizing tumours in clinical trials, so that, in determining the effectiveness of treatment, like may be compared with like.

RESPONSES OF DIFFERENT EXPERIMENTAL TUMOURS TO IRRADIATION IN RELATION TO THEIR CELLULAR RADIOSENSITIVITY *IN VITRO*

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Responses of tumours to single and fractionated radiation treatments may differ due to characteristics of the constituent tumour cells and due to the conditions in which these cells grow in the host. To analyse the relative importance of various factors and conditions for different tumours, cells from ten tumours in rats have been adapted to culture conditions (Barendsen, 1977). Using a clone selection procedure, cells were selected that can be inoculated in rats to produce tumours from which cells can be reproducibly titrated again in culture. Volume doubling times of the tumours ranged from 2.2 days to 10 days, while cell number doubling times *in vitro* ranged from 11 to 24 h. No systematic correlation between these two parameters could be established.

Sensitivities to 300 kV X rays varied considerably among cells from different tumours, with doses required to cause reproductive death in 50% of the cells ranging from 120 rad for cells from a lymphosarcoma to 430 rad for cells from a ureter squamous cell carcinoma (Barendsen *et al.*, 1977). Doses required to yield a growth delay of 20 days varied among different types of tumours from 400 rad to 2200 rad. No systematic correlation could be established with cellular sensitivity. It is concluded that information about a large number of factors and conditions at the cellular level is required to interpret responses of tumours to single and fractionated treatments.

REFERENCES

BARENDSEN, G. W., 1977. Radiosentitivity of tumours and derived cells in culture. *Biomedicine, 26*, 259–260.

BARENDSEN, G. W., JANSE, H. C., DEYS, B. F. and HOLLANDER, C. F., 1977. Comparison of growth characteristics of experimental tumours and derived cell cultures. *Cell Tissue Kinetics, 10*, 469–475.

Cardiovascular radiology

Chairman: Dr. W. Somerville

Recent advances in echocardiography, by S. Hunter.
Roles of radionuclides in myocardial infarction, by D. S. Dymond, A. T. Elliott, R. A. J. Spurrell and K. E. Britton.
An automated (heart) catheterization system (ACS), by V. H. de Villeneuve.
Transluminal dilatation of the iliac arteries, by G. J. van Andel and V. M. Krepel.

RECENT ADVANCES IN ECHOCARDIOGRAPHY

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Two growth points in the expanding field of cardiac ultrasound are the assessment of left ventricular function and the use of contrast echocardiography. Both techniques can be used to demonstrate underlying haemodynamic abnormalities with considerable clinical benefit.

Left ventricular function assessment using the single probe echo technique was initially based on accurate measurement of left ventricular cavity dimensions and assessment of mean rate of change of cavity size during the ejection phase (Feigenbaum, 1972; Kaye *et al.*, 1975). More recently digitization of left ventricular endocardial echoes has allowed calculation of peak rates of dimensional change during systole and diastole. These parameters are of value in left ventricular dysfunction and incoordinate contraction (Gibson and Brown, 1975) and can also be used to assess the severity of mitral valve stenosis. Provided access is available to a computer, the additional equipment for these methods is not expensive.

Contrast echocardiography depends on the production of microbubbles in fluids injected into the circulation centrally or peripherally. These microbubbles are short acting, harmless and reflect ultrasound intensely. Their presence is detected in the circulation by opacification of previously echo free cavities. Injections of indocyanine green, saline and blood have been successfully used to produce ultrasonic contrast studies but in our experience dextrose (5%) gives equally satisfactory opacification. Using peripheral venous injection of 1–2 ml of 5% dextrose in infants and small children it is possible to detect right to left intracardiac shunting and to determine the destination of the systemic venous return. In this way transposition of the great arteries may be readily differentiated from other causes of cyanotic congentital heart disease before catheretization (Mortera *et al.*, 1977).

REFERENCES

FEIGENBAUM, H., 1972. *Echocardiography* (Lee and Feabiger, Philadelphia).

GIBSON D. and BROWD, D. J., 1975. Measurement of left ventricular wall movement in man; comparison of echocardiography with angiography. *British Heart Journal, 37*, 677–683.

KAYE, H. H., TYNAN, M. and HUNTER, S., 1975. Validity of echocardiographic estimates of left ventricular size and performance in infants and children. *British Heart Journal, 37*, 371–375.

MORTERA, C., HUNTER, S. and TYNAN, M., 1977. Diagnosis of ventriculo arterial discordance (transposition of the great arteries) by contrast echocardiography. *British Heart Journal, 37*, 844–846.

ROLES OF RADIONUCLIDES IN MYOCARDIAL INFARCTION

By D. S. Dymond, A. T. Elliott, R. A. J. Spurrell and K. E. Britton

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The clinical role of radionuclides in the syndrome of myocardial infarction encompasses the acute event, the ensuing complications, and the screening of at " risk" populations. An acute infarct may be imaged by "hot" spot agents such as technetium 99^{m} stannous pyrophosphate (Tc PYP) that are infarct avid, or by "cold" spot agents such as the monovalent cation potassium analogues, *e.g.* thallium^{201}. The former, in which acutely necrotic muscle appears as an area of increased tracer uptake, detects recent infarction only. The techniques when performed after the first 24 hours following infarction, is highly sensitive for detecting and localizing transmural infarction, the detection of non transmural infarction having a variable repeated detection rate. Limitations of the method include poor results in the first 24 hours (although this may be overcome with newer agents such as imidodiphosphonate (IDP)), false positives due to persistent blood pool activity, and the lack of accurate *in vivo* infarct quantitation.

An infarct cannot be differentiated from an ischaemic area on a single thallium^{201} image, and sequential imaging is required as only an infarct will produce a permanent defect. Cold spot scanning is unable to determine whether an infarct is old or new, and is thus of limited value in diagnosing acute infarction. The advantage over the hot spot technique is the ability to detect perfusion defect within the first few hours of infarction, whereas hot spot scanning within the first twelve hours has a limited sensitivity with PYP.

In current clinical practice, infarct avid imaging agents such as Tc PYP, or the newer imidodiphosphonate which has a greater myocardial extraction and faster clearance from the blood pool than Tc PYP, should be used when the diagnosis of infarction cannot be made from conventional tests (for example, when the ECG shows conduction defects), or in the rarer conditions such as myocardial contusion or right ventricular infarction.

The assessment of complications of infarction is directed towards analysis of wall motion by equilibrium—gated or first-pass technique allowing the temporal separation of right and left ventricular activity in the right anterior oblique projection. Diffuse hypokinesis can be differentiated easily from a localized aneurism.

Screening of "at risk" populations depends on the assessment of myocardial perfusion or wall motion under conditions of stress. Thallium^{201} is the most widely used agent for perfusion scanning, while first-pass radionuclide angiography is effective in the demonstration of wall motion abnormalities.

AN AUTOMATED (HEART) CATHETERIZATION SYSTEM (ACS)

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During heart catheterization a limited amount of data is acquired: pressures, oxygen (transported), blood flow and ventricular dimensions. But they represent an enormous amount of information when examined exhaustively. As time is usually lacking, data processing seems a logical consequence. Experience with an ACS (Philips) is reported. This comprises the following elements—physiological measuring system, a cardiological keyboard, an alphanumerical keyboard and their video display, a processor with 16K core memory and magnetic disc unit, an analogue video converter and a matrix printer. The cardiologist operates, he directs the sampling, the calculations and the display via the cardiological keyboard equipped with a heart contour diagram, function keys and numerical keys. Special provisions as sampling frequency of 250 cycles, the transposition program, pre-sampling, respiration-directed blood pressure calculation, on-line left ventricular pressure registration and coupling with the cine-frames etc give the ACS many options for haemodynamic studies in children as well as adults.

TRANSLUMINAL DILATATION OF THE ILIAC ARTERIES

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The purpose of transluminal dilatation (Dotter procedure) is to widen stenoses, due to atheroma, with the aid of catheters or balloon catheters inserted into an artery according to the Seldinger procedure. In this way the atheromatous mass is compressed and remodelled against the arterial wall. Iliac arteries are especially suitable for transluminal dilatation. Examination before and after treatment includes history, physical examination and the determination of the systolic ankle blood pressure. The pre- and post-stenotic blood pressure tracings are recorded before and after dilatation, in order to measure the pressure gradient across the the stenosis. The technical procedure was illustrated diagrammatically. In four years 28 iliac stenoses were dilated in 25 patients. In two patients we failed to pass the stenosis with the guide wire. In two others, who were treated on both sides, there was no improvement in symptoms, although the objective data (systolic ankle blood pressure and angiography) indicated a disappearance of the stenosis. In the remaining cases (86%) the complaints disappeared or an improvement took place. The latter happened in four cases, in whom there was a total occlusion of the superficial femoral artery.

The conclusion is that the Dotter procedure is safe and from the patient's viewpoint it can be compared with the Seldinger procedure. The results are comparable with those obtained in reconstructive surgery.

Wide field and systemic irradiation

Chairman: Prof. M. J. Peckham
Total-body irradiations: physical aspects, by R. P. Parker.
Clinical aspects of total-body irradiation and bone-marrow grafting for radiosensitive tumours in man, by Ann Barrett.
Fractionated total-body irradiation on non-Hodgkin's lymphomas and chronic lymphatic leukaemia, by R. P. Symonds.
Total-body irradiation in advanced lymphosarcoma, by A. van Dijk-Milatz.
Half-body irradiation, by H. Bartelink and J. J. Battermann.
Wide-field irradiation for small-volume lymph-node metastases, by D. V. Ash.
Pulmonary irradiation for small-volume lung metastases, by K. A. Newton.

TOTAL BODY IRRADIATIONS: PHYSICAL ASPECTS

By R. P. Parker

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Various parameters requiring consideration when undertaking total-body irradiations were discussed with particular reference to the treatment-planning aspects. In practice most centres have to manage with the available equipment which was installed for other purposes; practical points resulting from this, such as reproducibility of set-up of patients and reliability were discussed. A review was given of reported techniques using single fields ranging from ^{60}Co to 25 MV X rays, as well as moving couch and multisource methods. It was concluded that although higher energies gave better dose distributions, a ^{60}Co unit using parallel opposed A.P. and P.A. fields was probably the best choice of equipment if low dose-rates were to be used bearing in mind reliability, clinical problems and dose distributions. A brief description was given of the large field ^{60}Co unit specially developed by the Physics Department of the Princess Margaret Hospital, Toronto, Canada.

CLINICAL ASPECTS OF TOTAL-BODY IRRADIATION AND BONE-MARROW GRAFTING FOR RADIOSENSITIVE TUMOURS IN MAN

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A historical review reveals that total body irradiation was first used as treatment for leukaemia and lymphoma in 1906. It is now used as part of the preparation for bone-marrow grafting in patients with leukaemia both to control disease and to produce immune-suppression. It is also used before grafting for some patients with aplasia who have failed to take a previous graft and in patients with radiosensitive tumours (such as Ewing's sarcoma).

For leukaemic patients before bone-marrow grafting, treatment consists of a total-body dose of 1000 rad (max), calculated from test doses given before the main treatment, measured with lithium fluoride dosimeters and checked by further measurement during the actual procedure. With our cobalt unit field sizes of 110 cm are obtained at four metres from the source giving a dose rate of 2.5 rad/min and total treatment times of approximately six hours. Patients are prepared for grafting with two days of intravenous cyclophosphamide (60 mg/kg) and sedated before irradiation with Chlorpromazine and Phenobarbitone. Steroids are given to reduce nausea and vomiting.

Side effects are minimal but may include nausea and mild vomiting, slight skin erythema, alopecia and parotitis; sterility and late cataracts may be expected. We have not seen any gut toxicity. Pneumonitis occurs in 50% of patients treated at Seattle and has a multifactorial pathogenesis with radiation graft versus host disease, immune depression and infection being implicated. Our policy is to graft patients with acute myeloid leukaemia in first remission. Early results from Seattle show 15 out of 22 patients surviving up to two years.

FRACTIONATED TOTAL-BODY IRRADIATION ON NON-HODGKIN'S LYMPHOMAS AND CHRONIC LYMPHATIC LEUKAEMIA

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Johnson and Ruhl (1976) reported that one third of patients suffering from progressive chronic lymphatic leukaemia (CLL) treated by total body irradiation (TBI) underwent a complete remission. Complete responders showed a recovery from immune paresis. In a randomized trial TBI was shown to be superior to Chlorambucil in the treatment of CLL.

Patients suffering from generalized lymphocytic lymphoma were treated in a randomized trial of TBI compared with combination chemotherapy (cyclophosphamide-vincristine-prednisolone–CVP) by Canellos *et al.* (1975). 84% partial responses and 56% complete responses were seen in the patients treat by TBI. Virtually identical results were reported in the group treated by CVP.

In Glasgow we treat patients with good marrow reserves with 15 rad (4 MV) twice weekly to 150 rad. Those patients with poor marrow reserves receive 10 rad twice weekly to tolerance.

We have only been using TBI for one year and have treated 11 patients, ten of whom have been failures after chemotherapy. We have found this treatment particularly valuable in patients with CLL who have developed an auto-immune haemolytic anaemia. All patients tolerated treatment well, the only side-effect seen being a depression of the platelet count.

REFERENCES

CANELLOS, G. P., DE VITA, V. T., YOUNG, R. C., CHABNER, B. A., SCHIEN, P. S. and JOHNSON, R. E., 1975. Therapy of advanced lymphocytic lymphoma. A preliminary report of a randomized trial of combination chemotherapy (CVP) and intensive radiotherapy. *British Journal of Cancer, 31, Suppl. II*, 474–479.

JOHNSON, R. E. and RUHL, U., 1976. Treatment of chronic lymphocytic leukaemia with emphasis on total body irradiation. *International Journal of Radiation Oncology, Biology, Physics, I*, 387–397.

TOTAL-BODY IRRADIATION IN ADVANCED LYMPHOSARCOMA

By A. van Dijk-Milatz

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A pilot study was initiated at the Department of Radiotherapy of the University of Utrecht to test total body irradiation (TBI) in advanced cases of lymphosarcoma. Thirty patients with generalized lymphosarcoma were entered into the study. Eleven patients had previously received local radiotherapy or chemotherapy, while 19 patients had received no prior chemotherapy. The original diagnostic lymph-node biopsies were reviewed and classified according to the Rappaport classification of non-Hodgkin's lymphomas. The thirty patients accepted were either stage III (6) or stage IV (24) and were staged according to the Ann Arbor system. Patients were treated on a 6 MeV linear accelerator at a distance of 600 cm from target to skin. The TBI course consisted of 10 rad in the midplane three times weekly to a maximal total dose of 300 rad. Toxicity caused by TBI was confined to bone-marrow depression. Haematological toxicity may be severe but in non-leukaemic patients it is in general acceptable. Complete clinical and radiological regression of disease (complete remission) was achieved in ten primarily treated patients and in four secondarily treated patients. Results in patients with leukaemia treated by TBI were very poor. We do not intend to go on treating these patients. In non-leukaemic primarily treated patients we achieved ten complete remissions out of 13 patients (77%).

We therefore conclude that TBI is a helpful treatment in the management of advanced lymphosarcoma.

HALF-BODY IRRADIATION

By G. M. M. Bartelink and J. J. Battermann

Antoni van Leeuwenhoek Hospital,
Amsterdam, The Netherlands

In this paper the possible advantage of half-body irradiation was discussed. Experimental data on cell culture and human pulmonary metastases show that a single dose of 800 rad can reduce the number of tumour cells 0.5 to three decades and give a growth delay of 14 to 290 days.

In patients with diffuse dissemination of breast cancer a single dose of 800 rad to the upper and/or lower half-body was given to relieve pain. This was achieved completely in 60% of the patients and partially in 40%. Two patients died of a sepsis after half-body irradiation following aggressive chemotherapy.

Therefore this kind of irradiation seems to be a useful palliative treatment in these patients.

WIDE-FIELD IRRADIATION FOR SMALL-VOLUME LYMPH-NODE METASTASES

By D. V. Ash

Institute of Cancer Research and The Royal Marsden Hospital, London and Surrey

In spite of the fact that wide-field elective irradiation of regional lymph-node areas has been practiced for many years it is still uncertain whether it is of any value. There are, however, good reasons for thinking that this treatment may be beneficial.

1. The introduction of elective wide-field treatment for testicular seminoma and Hodgkin's disease has seen dramatic improvement in survival from these conditions.
2. Irradiation of bulky disease in lymph nodes has shown that these can be controlled by radiation alone and suggests that small-volume disease would respond at least as well.
3. Surgical series and lymphography studies reveal a high incidence of sub-clinical disease in regional nodes which might benefit from treatment.
4. Pre-operative radiation regimes have shown a reduction in the expected incidence of positive nodes compared with comparably staged non-irradiated patients.
5. The incidence of late node recurrences in head and neck cancer has been reduced by elective irradiation to the neck.

In spite of this logical basis for wide-field elective node treatment there is no clinical trial confirming its efficacy in terms of overall survival. In cancer of the cervix the Manchester trial (Cole, 1976) has shown no increase in survival when local treatment by radium alone was compared with radium plus pelvic radiation. In head and neck cancer elective neck irradiation has also failed to demonstrate increased survival and does not refute the view that a watching policy for the neck with surgery and radiation on demand is no worse than a policy of elective nodal irradiation.

In addition to the failure to show benefit there is the possibility of doing harm and there is evidence of an increase in morbidity when wide fields are used, particularly in the pelvic and para-aortic regions.

In order for elective wide-field lymph-node irradiation to be successful the primary must be controlled: the node deposits must be sensitive to a moderate dose of radiation: all likely disease must be included in the radiation field and the chances of distant metastases must be low: elective treatment must be better than on demand treatment: the treatment must have an acceptable morbidity.

There are almost certainly a number of patients who might benefit from wide-field elective node irradiation but, so far, they have not been identified and the value of a policy of routine elective treatment has not yet been proved.

REFERENCE

Cole, M. P., 1976. Treatment of early stage II carcinoma of the cervix by radium. *Proceedings of the Royal Society of Medicine*, *69*, 673–675.

PULMONARY IRRADIATION FOR SMALL-VOLUME LUNG METASTASES

By K. A. Newton

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Following whole-lung irradiation at Westminster Hospital in 1969 of patients with a wide range of metastatic tumours, valuable information was gained concerning the tolerance of pulmonary tissue to irradiation. In a small number of patients, anti-tumour effects were observed.

In the present study, 14 patients with osteosarcoma have been treated with 6–7000 rad of opposing field megavoltage irradiation followed approximately six months later by surgical ablation. During the last two and a half weeks of limb irradiation, by which time the tumour in the limb had received approximately 3500 rad, prophylactic lung irradiation was started using opposing field irradiation on the 6 MeV linear accelerator, 150 rad to the centre of the mediastinum five days a week for 13 treatments, to a total of 1950 rad. With increased penetration in pulmonary tissue the dose in the lungs was approximately 2400 rad.

Six of these 14 patients have survived for more than five years. This policy is an attempt to deal with small volume metastases undetectable by radiography and was abandoned some years ago with the advent of adjuvant chemotherapy. Because of the present results, it is considered reasonable to reopen the question of radiotherapy in eradicating small volume lung metastases.

Proceedings of the British Institute of Radiology

The Annual Congress, April 13–14, 1978. Scientific Exhibition

The radiology of angiodysplasia, by D. J. Allison.
Some uses of therapeutic vascular occlusion, by T. A. S. Buist.
Radiographic presentations of von Recklinghausen's disease, by E. S. Casselman and W. T. Miller (*no abstract received*).
Observer assessment of mammograms and an evaluation of the significance of radiographic patterns, by A. Chaffe, E. J. Roebuck and B. S. Worthington.
Recognition of surgical swabs, by G. de Lacey.
Effervescent granules for the barium meal, by G. de Lacey, B. Wignall and C. Bray.
Remote interpretation of radiographic images by closed circuit television link, by N. McGuire, F. Johnson and B. S. Worthington.
Radiological and histological correlation in congenital ear anomalies in anencephaly, by P. D. Phelps and J. L. Wright.
A teaching aid and guide for the basic understanding of transpositions and abnormalities of cardiac position, by J. F. Reidy.
Unusual signs for cholecystosis, by J. H. J. Ruijs.
Some bone changes in anaemia, by J. D. Stevenson.
Surgical revascularization of the cerebral cortex, by Jennifer M. Weller.
Ultrasonic diagnosis of gastrointestinal lesions, by E. Samuel and S. Holt.
Computed tomography in testicular teratomas, by Janet E. Husband, N. J. Hodson and D. Mears.
Art and artefact in computerized tomography, by Brenda M. Sandin and L. Kreel.
Radiation exposure to the patient in whole body computed tomography, by R. P. Parker and Pauline Hobday.
Internal morphological analysis by NMR imaging, by W. S. Hinshaw, E. R. Andrew, P. A. Bottomley, G. N. Holland, W. S. Moore and B. S. Worthington.
A range of test objects for evaluating the performance of CT machines, by D. R. White, R. D. Speller, P. M. Taylor, R. Darlison, A. Rickwood and B. Horn.
Simulix-simulator with simtomix, by W. Hogervorst (*no abstract received*).
Whole body scanner: treatment planning project, by K. Cassell, Pauline Hobday, N. Hodson, Janet Husband, R. P. Parker and J. Macdonald (*no abstract received*).
Cellular DNA and proliferation in radiotherapy of cervical cancer, by B. Dixon and C. J. Carter.
A simple inexpensive data processing system for radiotherapy departmental notes, by M. J. Ostrowski and A. W. Jackson.

THE RADIOLOGY OF ANGIODYSPLASIA

By D. J. Allison

Hammersmith Hospital and Royal Postgraduate
Medical School, Du Cane Road, London, W.12

The term angiodysplasia refers to microvascular abnormalities of the bowel wall which can cause gastro-intestinal bleeding (Galdabini, 1978; Boley *et al.*, 1977). The lesions cannot be demonstrated by barium studies or endoscopy, and can neither be seen nor felt by the surgeon at laparotomy.

Selective visceral angiography is necessary to diagnose angiodysplasia, and postoperative radiology of the resected bowel is usually necessary to localize the lesions for histological examination (Tarin *et al.*, 1978).

Angiodysplasia was found by preoperative selective visceral angiography in eight out of 12 patients who presented at Hammersmith Hospital over a period of four years with unexplained recurrent bleeding from the gastro-intestinal tract. Postoperative angiography of the resected portion of bowel localized the abnormal areas for histological study which revealed a variety of microvascular abnormalities including arteriolar, capillary, venular and arterio-venous malformations. While angiodysplasia is a useful descriptive radiological term it does not, therefore, represent a single pathological entity.

REFERENCES

Galdabini, J. J., 1974. Case records of the Massachusetts General Hospital. *New England Journal of Medicine*, *291*, 569.

Boley, S. J., Sammartano, R., Adams, A., Dibiase, A., Kleinhaus, S., and Sprayregens, S., 1977. On the nature and etiology of vascular ectasias of the colon. *Gastroenterology*, *72*, 650–660.

Tarin, D., Allison, D. J., Modlin, I. M., and Neale, G., 1978. Diagnosis and management of obscure gastrointestinal bleeding. *British Medical Journal*, *2*, 751–754.

SOME USES OF THERAPEUTIC VASCULAR OCCLUSION

By T. A. S. Buist

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Royal Infirmary of Edinburgh, EH3 9YW

Modern selective angiography can localize a focus of active arterial bleeding or define the blood supply of a vascular malformation. Catheter techniques can now be extended to produce selective vessel occlusion by introduction of balloon catheters or emboli materials to arrest bleeding or obliterate a vascular malformation.

Experience with focal bleeding in the kidney particularly has confirmed the advantage of this procedure as an alternative to surgery. For persistent post biopsy renal haemorrhage it is the treatment of choice.

In the management of highly vascular renal tumours, preoperative arterial occlusion can assist and improve surgical technique. Renal artery embolization is an alternative to palliative nephrectomy when the disease is advanced.

Bleeding from lesions in many other areas, such as bladder and uterus have also been effectively controlled by selective arterial embolization.

Using a percutaneous transhepatic approach, catheterization of the portal and splenic veins, and embolization of branches which supply gastro-oesophageal varices, is an effective emergency procedure for the control of variceal haemorrhage in portal hypertension.

Representative examples of our experience of vascular occlusion in 21 patients were illustrated. The occlusive materials used were balloon catheters, wire coils with cotton and woollen threads, and gelatin sponge (Sterispon) alone, or with added sodium tetradecyl sulphate (STD).

Proceedings of The British Institute of Radiology

OBSERVER ASSESSMENT OF MAMMOGRAMS AND AN EVALUATION OF THE SIGNIFICANCE OF RADIOGRAPHIC PATTERNS

By A. Chaffe, E. J. Roebuck and B. S. Worthington

University of Nottingham

Receiver operating characteristic curves have been shown to be a valid and objective method of measuring observer performance in reading mammograms. These curves plot the conditional probability of true positive against false positive results as the confidence threshold of the observer varies. The area under the graph measures observer sensitivity or the ability to perform the task correctly. Bias values give an indication of the overall confidence of the observers in making their decisions, serial measurements allowing identification of observers who show extremes of optimism or pessimism, or who change their decision criteria and would be unreliable as screeners.

In a comparative study of a surgically referred group and a self referred group from a screening clinic the incidence of radiographic parenchymal patterns (Wolfe classification) has been examined. The higher incidence in patients with neoplasm of the P2 and DY types as compared with the N1 and P1 types first shown by Wolfe in 1976 has been confirmed. Of the two patterns designated high risk, P2 correlates with the known risk factors of age at first child and increasing parity, whereas DY does not.

RECOGNITION OF SURGICAL SWABS

By G. de Lacey

X-ray Department, St. George's Hospital, London

The efficiency of theatre protocol is the most important safeguard against a swab or pack being retained during an operation. Nonetheless, mistakes do occur and may be compounded when the radiologist does not recognize a retained pack because he is not familiar with the marker pattern. Most packs have a different marker appearance than do swabs. Pack markers are usually in the form of an opaque band or strip whereas swab markers appear as long thin filaments. Two types of barium-impregnated markers are used in the United Kingdom, one made of yarn and the other of plastic (polyvinyl chloride). The advantage of yarn over plastic is that it has a softer feel and it does not become brittle if sterilized more than once. For these reasons some surgeons prefer swabs or packs marked with yarn. Although 55% w/w barium sulphate is specified by the British Pharmacopoea to be used as the marking substance, yarn cannot carry as much barium sulphate without losing much of its tensile strength. For this reason, yarn filament markers are of reduced radiodensity. Most markers manufactured in the United Kingdom are the high radiodensity plastic type, and even the less dense yarn markers will be clearly recognizable to the trained observer. However, some markers produced by Continental manufacturers are very poorly opaque and may be difficult to detect. Very small swabs may also be difficult to visualize if projected over bone, films are under-exposed, or the patient is breathing. The exhibit illustrated cases of retained packs which were not recognized because of unfamiliarity with the marker pattern. The radiographic appearance of the common swab and pack markers in use in the UK were demonstrated.

EFFERVESCENT GRANULES FOR THE BARIUM MEAL

By G. de Lacey, B. Wignall and C. Bray

Radiology and Pharmacy Departments
St. George's Hospital, London

A simple cheap, efficient method of producing gas for the double contrast barium meal was illustrated. A granulated powder containing sodium bicarbonate and citric acid was prepared in the hospital pharmacy, and samples were provided. The formula and method of producing the granules, which are easy to chew, was described.

REMOTE INTERPRETATION OF RADIOGRAPHIC IMAGES BY CLOSED CIRCUIT TELEVISION LINK

By N. McGuire, F. Johnson and B. S. Worthington

University of Nottingham

The faithful reproduction of radiographs transmitted through a closed circuit television is limited by the extent to which the grey scale in the original film can be reproduced (dynamic range of the television picture); the number of lines in the television raster (625) and the bandwidth of the system (6.5 MHz) which together limit the resolution which can be achieved and also the extent of observer interaction in altering image size, brightness and contrast.

The best perceptible resolution on direct viewing of a radiograph of a line pair phantom was 10 line pairs/mm compared with 1.59 line paris/mm in the transmitted image.

Using receiver operating characteristic curve analysis the effect of these limitations on observer performance was assessed in respect of gamma camera images of a phantom containing a cold spot, randomly placed within a flood field. The reduced sensitivity observed was reflected in a high error rate particularly in detecting low density foreign bodies during a simulated casualty reporting session.

The TV system here assessed is quite unacceptable for use in giving definitive reports on radiographs and only provisional statements can be made. It could well be used for checking remotely the quality and completeness of any examination, however, and appropriate advice given.

RADIOLOGICAL AND HISTOLOGICAL CORRELATION IN CONGENITAL EAR ANOMALIES IN ANENCEPHALY

By P. D. Phelps and J. L. Wright

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Walsgrave, Coventry CV2 2DX

The ear in anencephaly is always abnormal and shows features of malformation seen also in children with congenital ear anomalies. Tomographic and histological sections of anencephalic temporal bones were demonstrated. Ossicular abnormalities similar to those found at operation for congenital conductive deafness were shown, as well as a wide range of structural abnormalities of the labyrinth and internal auditory meatus. Distortion of the cochlea with varying degrees of underdevelopment of the bony spiral similar to these anencephalic examples, may be demonstrated by tomography in some severely deaf children and help in their assessment.

A TEACHING AID AND GUIDE FOR THE BASIC UNDERSTANDING OF TRANSPOSITIONS AND ABNORMALITIES OF CARDIAC POSITION

By J. F. Reidy

Department of Radiology, St. George's Hospital, London SW17

To all except the specialist working with congenital heart disease, understanding transpositions and abnormalities of cardiac position is likely to prove difficult. The situation is not helped by the great variety of terms used and the lack of any standard terminology. A model was demonstrated which consists of a Perspex egg-shaped frame (the heart), into which fit interlocking pieces (atria, ventricles and great vessels). The pieces are double-sided and identifiable only by their morphology. The positions can be changed around or reversed so that all the possible anomalies can be easily "put together" and demonstrated. An account of fundamental morphology, definitions and the most usual terminology was included.

A separate "liver" piece which is also reversible can be placed below the heart. It is so coloured that it will match the lateral arrangement of the atria if the rule of viscero-atrial situs is applied. The frame can be swung to the left (laevocardia) or to the right (dextrocardia) quite independently of whatever anomaly is demonstrated within the frame.

There are rare exceptions where use of the model breaks down, but in most cases it can be used to demonstrate both the relationships and connections of the chambers and great vessels. In addition, it helps relate the plain chest film findings to these various anomalies.

UNUSUAL SIGNS FOR CHOLECYSTOSIS

By J. H. J. Ruijs

University Hospital, Utrecht, the Netherlands

Cholecystosis—especially adenomyomatosis and cholesterolosis—can often be diagnosed if contrast-filled Rokitansky-Aschoff sinuses and other well defined irregulatiries are visible.

In this exhibition seven cases of cholecystosis were presented with only minor and unusual signs which can be detected by the alert eye of the radiologist—in some instances—with the help of functional investigation of the gall-bladder.

SOME BONE CHANGES IN ANAEMIA

By J. D. Stevenson

Royal National Orthopaedic Hospital, London W1

Radiological bone changes in anaemia are limited mainly to two: sickle cell disease and thalassaemia. The changes are those of bone marrow expansion and as much, are non-specific although bone infarcts and salmonella osteomyelitis occur in sickle cell disease, and extramedullary haemopoiesis is seen in thalassaemia. Examples to display the classic features of the two entities were shown.

SURGICAL REVASCULARIZATION OF THE CEREBRAL CORTEX

By Jennifer M. Weller

Department of Radiology,
North Manchester General Hospital,
Crumpsall, Manchester M8 6RB

Pre- and postoperative cerebral angiograms were presented to illustrate this surgical technique which is currently being evaluated. End to side anastomosis of a branch of the superficial temporal artery to a cortical branch of the middle cerebral artery is performed through a small craniotomy. Postoperative angiograms at six weeks demonstrate in these cases patency of the intracranial–extracranial shunt with retrograde refilling of middle cerebral artery branches.

The cases chosen both presented evidence of cerebral under-perfusion secondary to major vascular occlusion which is put forward as a good indication for this type of surgical procedure. Neither case had evidence of established infaction.

ULTRASONIC DIAGNOSIS OF GASTROINTESTINAL LESIONS

By E. Samuel and S. Holt

Royal Infirmary of Edinburgh

Thickened bowel may produce a recognizable pattern on ultrasound examination and the present study was undertaken to evaluate the potential of grey-scale ultrasound in the assessment of ileo-caecal Crohn's disease, thereby perhaps obviating the need for repeated abdominal X-rays, after the initial diagnosis has been made. Grey-scale ultrasound was performed in 17 patients with Crohn's disease of varying extent and severity. In 13 of the 17 patients studied, thickening of the wall of the terminal ileum and caecum, with adjoining inflammatory changes in the mesentery, produced recognizable patterns on longitudinal and transverse ultrasonographs. Three main ultrasound images were identified, corresponding to thickened and stenosed bowel, matted coils of bowel and a combination of the two with adjacent abscess formation.

Although not providing the specificity or detail of conventional radiology, grey-scale ultrasound can be helpful in the assessment of ileo-caecal Crohn's disease, particularly in younger patients, where radiation hazards should be kept to a minimum.

COMPUTED TOMOGRAPHY IN TESTICULAR TERATOMAS

By Janet E. Husband, N. J. Hodson and D. Mears

The Royal Marsden Hospital and Institute of Cancer Research, Sutton, Surrey

CT scan findings in 46 patients with malignant teratoma are presented. The lungs, mediastinum and abdomen were examined in all patients.

The results of this study indicated that CT is more sensitive than whole lung tomography in detecting pulmonary metastases. Lymphadenopathy was demonstrated in the mediastinum in three patients of this series in whom conventional radiology was normal.

CT findings in the abdomen were compared with those of lymphography in all patients.

There was good correlation between these techniques but

CT has the advantage of defining the full extent of disease more precisely than lymphography alone.

CT has also been used to monitor response to chemotherapy and radiotherapy. Since the liver is demonstrated on all upper abdominal scans, CT has been used to evaluate the presence of liver metastases. These were demonstrated in three out of 46 patients.

ART AND ARTEFACT IN COMPUTERIZED TOMOGRAPHY

By Brenda M. Sandin and L. Kreel

Division of Radiology, Clinical Research Centre, Harrow

Like all radiographic equipment, computerized tomographic units produce artefacts. These can be caused by change in the environmental temperature, by electronic noise and by mechanical problems of the scanner itself. Similarly, materials of high density within the body can produce striking results.

Environmental temperatures, such as high room temperature, cause striped linear bands and random patterns, described as "wallpaper" and "weetabix".

Electronic noise destroys the scan data and occurs when there is electronic component overheating, presenting as "light-up" areas or as the random "wallpaper" and "weetabix" pattern.

Mechanical problems resulting from mechanical faults in the scanner interfere with reconstruction and take the form of spinning catherine wheels.

High density materials, such as metallic implants and contrast media produce stellate artefacts of great intensity with centres of alternating black and white rings.

RADIATION EXPOSURE TO THE PATIENT IN WHOLE BODY COMPUTED TOMOGRAPHY

By R. P. Parker and Pauline Hobday

The Royal Marsden Hospital
Downs Road, Sutton, Surrey SM2 5PT

The work described in this exhibit has been published in *The British Journal of Radiology*, *51*, (1978) p. 925).

INTERNAL MORPHOLOGICAL ANALYSIS BY NMR IMAGING

By W. S. Hinshaw, E. R. Andrew
P. A. Bottomley, G. N. Holland, W. S. Moore
and B. S. Worthington

University of Nottingham

NMR is a well-established method of studying the properties of materials at the molecular level. The technique has recently been applied to studying the internal structure of biological material by mapping the distribution of the density of protons especially those with considerable thermal motion in cellular water and lipids.

The apparatus has an 8 cm sample chamber mounted within a large magnet and a 30 MHz NMR spectrometer operating in the pulse Fourier transform mode which is used to excite and observe the resonance phenomenon.

Coronal NMR sections through the head and forelimbs of a rabbit are shown with the corresponding anatomical sections, followed by a transverse NMR section through the wrist of one of the authors with a representative cadaver section. The dark areas correspond to regions of high mobile proton density such as marrow and fat; the light areas to low proton density as in cortical bone and tendons. As with CAT scanning resolution of soft tissue detail is at a premium but NMR imaging is not confined to the transverse plane and any plane in any orientation can be selected. There are grounds for anticipating that NMR will be more than a mere alternative to CAT scanning for it may prove possible to achieve a useful degree of tissue discrimination and characterization by analysing components of the complex NMR signal.

A RANGE OF TEST OBJECTS FOR EVALUATING THE PERFORMANCE OF CT MACHINES

By D. R. White,* R. D. Speller,† P. M. Taylor,*
R. Darlison,* A. Rickwood* and B. Horn†

**Radiation Physics Department*
St. Bartholomew's Hospital and
†*Department of Physics as Applied to Medicine,*
Middlesex Hospital Medical School, London

A comprehensive range of test objects based upon high precision tissue substitutes has been developed specifically for CT scanners. Evaluation plugs for resolution, sensitivity, slice thickness, etc may be inserted into regular geometry and realistic skull, abdomen and thorax sections. The range of test objects were shown together with some typical results.

CELLULAR DNA AND PROLIFERATION IN RADIOTHERAPY OF CERVICAL CANCER

By B. Dixon and C. J. Carter

Cookridge Hospital, Leeds

Two techniques were illustrated for the determination of the cellular kinetic status of pretreatment tumour biopsies obtained from patients referred for radiotherapy for carcinoma of the cervix. The first involved the use of tritiated thymidine and incubation of biopsies within a hyperbaric oxygen capsule and the second the imprinting of cells on microscope slides followed by measurement of nuclear DNA, by Feulgen photometry with a Vickers M85 flying spot microdensitometer. Data obtained by the two techniques were compared and related to follow-up studies of patients for up to two years following radiotherapy.

A SIMPLE INEXPENSIVE DATA PROCESSING SYSTEM FOR RADIOTHERAPY DEPARTMENTAL NOTES

By M. J. Ostrowski and A. W. Jackson

Department of Radiotherapy and Oncology,
Norfolk and Norwich Hospital, Norwich

The Norwich Radiotherapy and Oncology Centre, which serves the population of Norfolk, receives patients from a number of hospitals in the region which each have their own internal note system, so that an individual patient may have up to four independent sets of notes. The department maintains its own note system in order to provide continuity of care for these patients. This has produced a storage problem which was exacerbated when plans to build a new department were abandoned due to economic factors.

The departmental notes are used to record basic details of the patients, the diagnosis, and a treatment summary as well as follow-up annotations on progress and additional therapy. Quick access is essential to answer enquiries and deal with emergencies. Our problem has been solved by adapting an Olivetti word processing system. This consists of an electric typewriter which can automatically type at a speed of 150 words per minute, two high capacity external memories containing 250,000 characters each on interchangeable magnetic tape cartridges, a control console consisting of eight push-buttons with built-in lights which set the system in its different working modes and four signalling lights to indicate the appropriate function in use, and a central unit controlling the operations of the machine in accordance with the operator's instruction.

The basic information on the patient and the treatment summary is broken down into 15 separate headings, using a very simple standard form of abbreviation. These headings are typed into the machine to be stored and later reproduced as a single line entry of 84 characters, the machine being able to sort on 60 of these characters. A treatment processing form is completed for entering onto tape when all new patients have completed their primary therapy, so that an updated record of all new patients attending the department is maintained. A second tape is used to store follow-up annotations which are summarized at regular intervals.

The advantages of this system are:

1. It is inexpensive compared with a dedicated computer.
2. It does not require a special program, so that errors due to coding are eliminated.
3. The simplicity of the system means that no specially trained staff need to be employed and that all members of the department can use it.
4. The equipment is easy to operate and the typewriter can be used when the word processor is not needed.
5. The departmental storage problem has been solved and two years intake of new patients can be held on one tape.
6. The machine is able to print basic details of the patients instantly and information can be retrieved and updated as and when necessary.
7. A spare tape can be made in case of accidents and stored in another part of the department or hospital.
8. The "standard letter facility" on the machine can be used for writing reports and scientific papers which often require repeated correction before the final version is reached. The draft report is stored on tape. Any amendments, deletions or corrections can be typed in so that a fair copy in context can be produced at any time, the modifications being inserted automatically.
9. Finally, the machine can be used for departmental research, enabling one to obtain lists of patients undergoing a specific therapy or of patients with a particular disease state, so that the quality of work performed by the department should improve as a result.

Book review

Radiation-Associated Thyroid Carcinoma. Edited by L. J. DeGroot, L. A. Frohman, E. L. Kaplan and S. Refetoff, pp. xx + 539, illus., 1977 (Grune & Stratton, Inc., New York), $17.50.

This book is the published proceedings of a workshop conference held at the University of Chicago in late 1976. There are over 40 different papers grouped into the 12 main sections plus discussion and panel reports and summaries. The participants were almost entirely from North America and included most of the well known American experts on thyroid disease and in particular those associated with the investigation of patients potentially at risk from childhood irradiation.

The main subject headings concern the scanning programmes of patients at risk, useful general discussion of the staging and classification of thyroid tumours in general and their natural history and then the more contentious matter regarding the real nature of these "occult" micro-tumours which seem to run such a benign course. Much of the information has already been published elsewhere in medical journals but is here summarized and occasionally up-dated to give a useful collection of work on the subject.

The association with childhood irradiation—usually of the thymus, tonsils and adenoids or skin conditions, was first recognized in 1950 and is entirely associated with papillary tumours. No medullary or anaplastic carcinomas were seen. The scanning programmes have also shown an increased number of parathyroid adenomas than would be expected.

Though various points of view are expressed in these papers and discussion, there is a clear majority feeling that these "occult" carcinomas—usually only a few millimetres in diameter (whether they are radiation induced or not), do not seem to run a malignant course and the tendency now is for less drastic surgery than was at first advised. By the time nodular lesions are palpable or visible on scan, they are no longer "occult" and active therapy is then certainly called for.

The book provides a most useful up-to-date collection of views of acknowledged experts and the panel reports provide a summarized and generally acceptable view of the whole problem. They are not necessarily unanimous and where conflicting opinions are held this is still made clear in these reports. It is also recognized that future work and longer follow-up may produce new facts and alter current attitudes.

It is perhaps unavoidable that such a work lacks an index but the lack of running (page) headings does not help one in finding one's way through the book. Nevertheless this book provides a most useful summary in balanced form of the whole question of thyroid carcinoma linked to childhood irradiation of the head and neck and is to be commended as a valuable compilation to all workers in this field.

D. H. KEELING.

Forthcoming events and other notices

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).

Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

An Advanced Course in Cardiac Ultrasound

This course, to be held at Harefield Hospital, April 23–27, 1979, is intended for doctors and technicians already working in the field or with some knowledge of the subject. It will be under the direction of Ronald Pridie and Stuart Hunter. Other speakers will include Derek Gibson, Grahame Leach, Robert Anderson, John Gore and Dan Thunstall-Pedoe.

Residential accommodation is available. Applications to: Mrs. L. Grieve, Ultrasound Department, Harefield Hospital, Harefield, Middlesex.

1979 The British Institute of Radiology Annual Congress

The 37th British Institute of Radiology Annual Congress and Scientific Exhibition will be held at the Middlesex Hospital Medical School on April 26–27, 1979. Included in a programme of invited papers on diagnosis, therapy, radiological physics and nuclear medicine topics will be the Presidential Address by Mr. W. M. Ross entitled *The Institute, yesterday and tomorrow,* and the Silvanus Thompson Memorial Lecture by Professor G. E. Adams on *Past, present and future of hypoxic cell sensitizers.*

Details and registration from The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG.

Conversazione

The British Institute of Radiology Conversazione will be held at the new Royal College of Radiologists house at 38 Portland Place, London on May 16, 1979.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

European Congress of Xeroradiology

A congress of xeroradiology organized by the Fondazione Internazionale Menarini will be held in Venice, Italy from May 11–13, 1979 inclusive.

The three day programme will include invited and proffered papers and teaching seminars on all aspects of xeroradiographic techniques, imaging and directions of future development.

Further information may be obtained from the Organizing Committee, European Congress of Xeroradiology, Dott. ssa Angela Peroni, Fondazione Menarini Internazionale, Piazza Del Carmine 4, 20100 Milan, Italy.

Third European Nuclear Medicine Society Meeting

This meeting will be held in Karlovy Vary, Czechoslovakia, May 15–18, 1979 and is organized by the Czechoslovak Society of Nuclear Medicine and Radiation Hygiene.

The official languages will be English, French, German and Russian and simultaneous interpretation will be provided.

Registration: Czechoslovak Medical Society, J. E. Purkyne, 3rd European Congress of Nuclear Medicine, Sokolská 21, 120 26 Praha 2, Czechoslovakia.

Mackenzie Davidson Memorial Lecture

To be given by Dr. G. B. Schofield, Medical Officer, British Nuclear Fuels Ltd., on *Biological control in a plutonium production facility* at The British Institute of Radiology, 32 Welbeck Street, London, W1 on Thursday, May 17, 1979.

Paediatric Radiology

A two-day course in diagnostic paediatric imaging will be held at the Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London, WC1 on May 17–18, 1979. The main theme of this course will be the thorax.

Further details and application forms are available from The Secretary, Department of Paediatric Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JN.

23rd Crookshank Lecture

The 23rd Crookshank Lecture on Genetic Engineering and Public Concern will be delivered by Sir Gordon Wolstenholme O.B.E., F.R.C.P., at 66 Portland Place, London at 4.30 p.m. on Friday May 18, 1979. The Chair will be taken by the President of the Royal College of Radiologists, Professor R. E. Steiner M.D., F.R.C.P., P.R.C.R. The lecture, which is open to all members of the medical profession, will be preceded by the admission of Fellows. Refreshments will be served from 4.00 p.m. and admission is free without tickets.

International Symposium on Interventional Radiology

An E.A.R. Symposium, organized by the Portuguese Society of Radiology and Nuclear Medicine, will be held May 30–June 2, 1979 in the Algarve, Portugal.

Proposed sessions include vascular therapy; selective embolization and management; catheter implantation in chemotherapy and percutaneous treatments; ultrasonic guiding techniques and nuclear imaging as a guiding technique for biopsy and fluid aspiration.

For further information contact the Portuguese Society of Radiology and Nuclear Medicine, 123, 1.° Esq., Avenida Elias Garcia, Lisbon 1, Portugal.

Nuclear Cardiology

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology, to be held on June 20, 1979 at St. Bartholomew's Hospital, Gloucester House, Little Britain, London, EC1. Anyone wishing to make a presentation should contact Dr. K. E. Britton, St. Bartholomew's Hospital.

Further information regarding this meeting can be obtained from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01–935 6237).

International Skeletal Society

Tne International Skeletal Society announces the 6th annual refresher course, August 31–September 2, 1979 at the München Sheraton Hotel, München, Bavaria, Federal Republic of Germany. Fees: US$250; residents and registrars US$125; US$100 for one-day attendance. Speakers are outstanding scientists in the field of radiology, pathology and orthopaedic surgery.

Chairman: Prof. Dr. F. Heuck, Kriegsbergstr. 60, D-7000 Stuttgart 1.

Contact: Interplan-Kongressdienst., Sophienstr. 1, D-8000, München 2.

Forthcoming events

IV EUROPEAN CONGRESS OF RADIOLOGY

The IV European Congress of Radiology will take place in Hamburg (German Federal Republic), September 4–8, 1979.

Scientific programme:

diagnostic research of organs of the upper abdomen;
diagnostic research in nuclear medicine: organs of the upper abdomen;
radiotherapy in tumours of the genital system of males and females;
radiobiology and X-ray protection (combined therapies and risks of ray exposure);
radiophysics and techniques (methodical problems in diagnostics and in planning of radiotherapy).

Enquiries: Secretary of the IV European Congress of Radiology, Postfach 10 64 07, D-2000 Hamburg 1, Federal German Republic.

QUANTITATION OF TUMOUR RESPONSE: A CRITICAL APPRAISAL

The L. H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to stimulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.
Factors of prognostic significance.
In vitro assays of tumours excised after treatment *in vivo*.
The choice of suitable experimental models in rodents.
The role of human tumour xenografts.
Statistical evaluation of tumour response data.
The limitations and artefacts of each assay technique.
The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

SYMPOSIUM ON SPINE AND ITS CONTENTS

E.A.R. "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in the:

(a) Equipments and investigative methods of spine and spinal cord.
(b) Radioanatomy and physiology of spine and spinal cord.
(c) Radiodiagnosis of pathological conditions.
(d) Interventive (diapeutic) radiodiagnostic methods.

For further information contact (not later than June 1979): The secretariate of "Vertebro 1980", P.O.B. 88, Sokolská 31, 120 26 Praha 2, Czechoslovakia.

XV INTERNATIONAL CONGRESS OF RADIOLOGY

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The Scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Further information from: Secretariat ICR-81, Ave. Winston Churchill 234B-Box 16, B-1180 Brussels, Belgium.

Corrigendum

The following misprint has been noted. Hyperbaric oxygen and radiotherapy: A Medical Research Council trial in carcinoma of the cervix; BRITISH JOURNAL OF RADIOLOGY, *Vol.51*. November, 1978, page 882, Table V:
The first figure in the final column appearing as 0.034 should in fact read 0.34.

We apologize for this error.

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Radiology study guide 335
Radiation-associated thyroid carcinoma 350

Book received

Receipt of the following book is acknowledged as a courtesy to the sender. This publication has been lodged in the Library of The British Institute of Radiology for the use of members.
Prevention and Detection of Cancer. Part 1—Prevention. Volume 2—Etiology · Prevention Methods. Edited by H. E. Nieburgs, pp. xix+1205, illust. (Marcel Dekker Inc., New York and Basel), 1978, Sw. Fr. 190. ISBN 0-8247-6682-2.

Medical Chart received

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BIRKNER'S RADIOLOGICAL CHART OF THE HUMAN SKELETON (Urban & Schwarzenberg, Munich) DM58.

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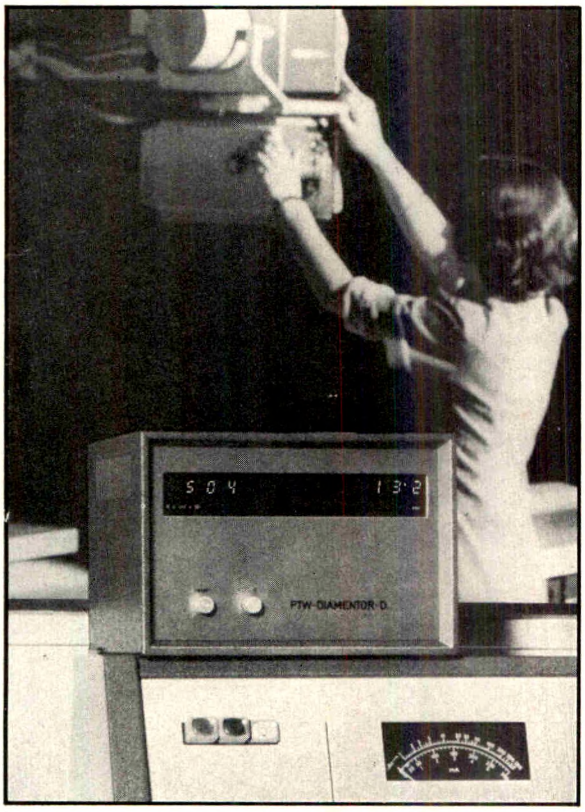

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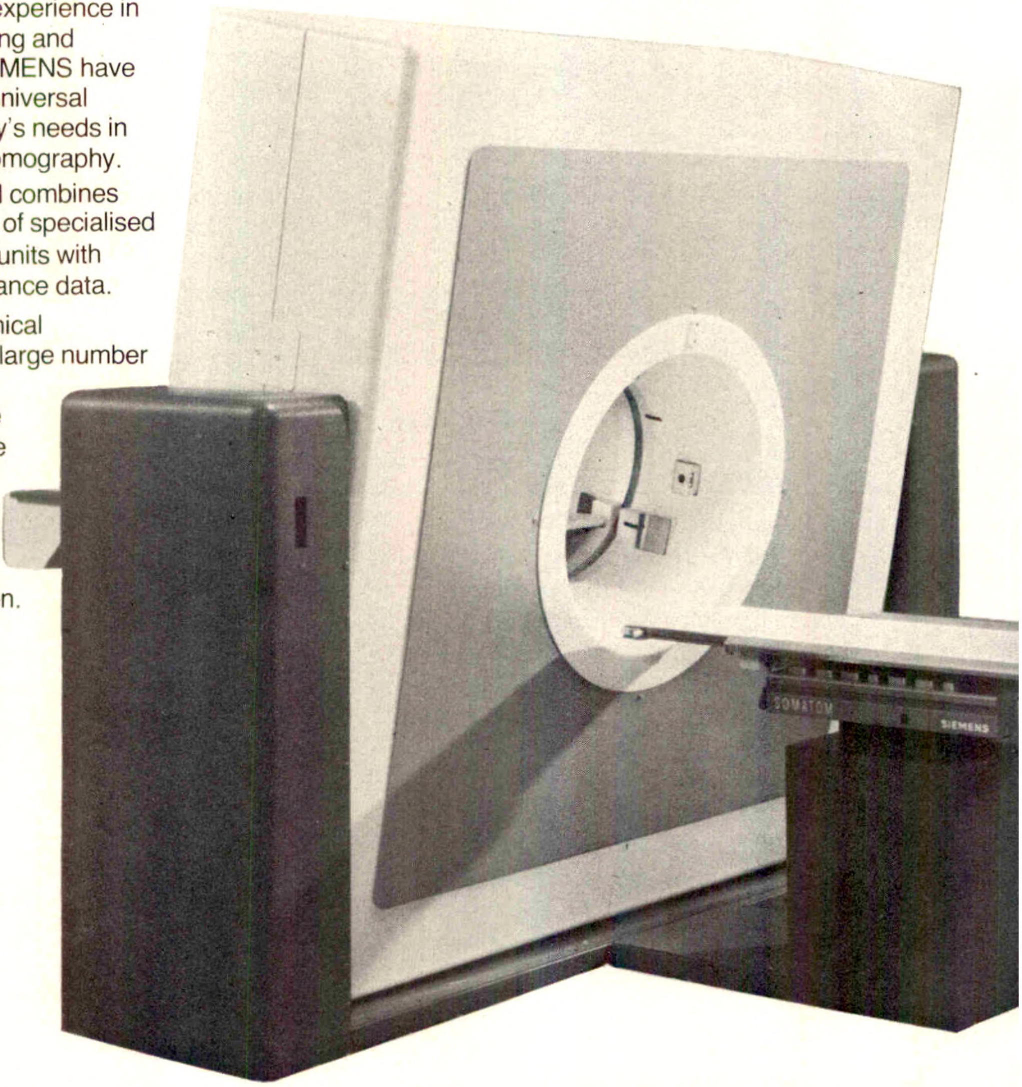

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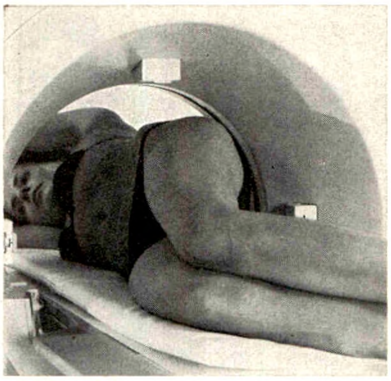

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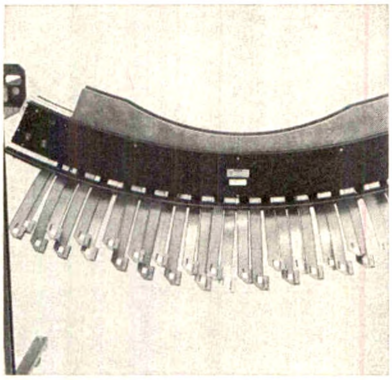

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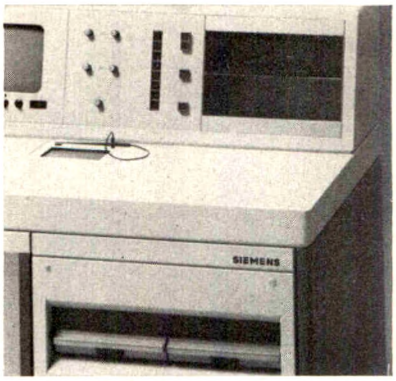

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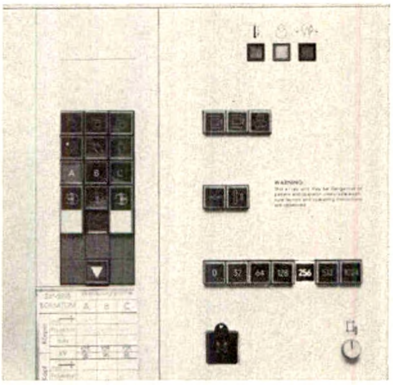

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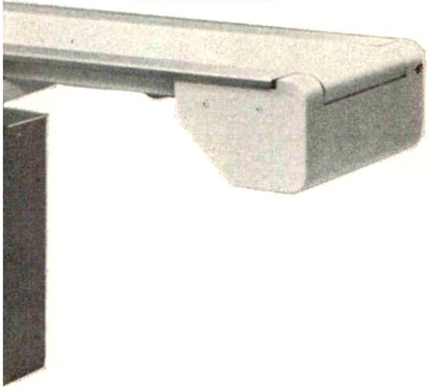

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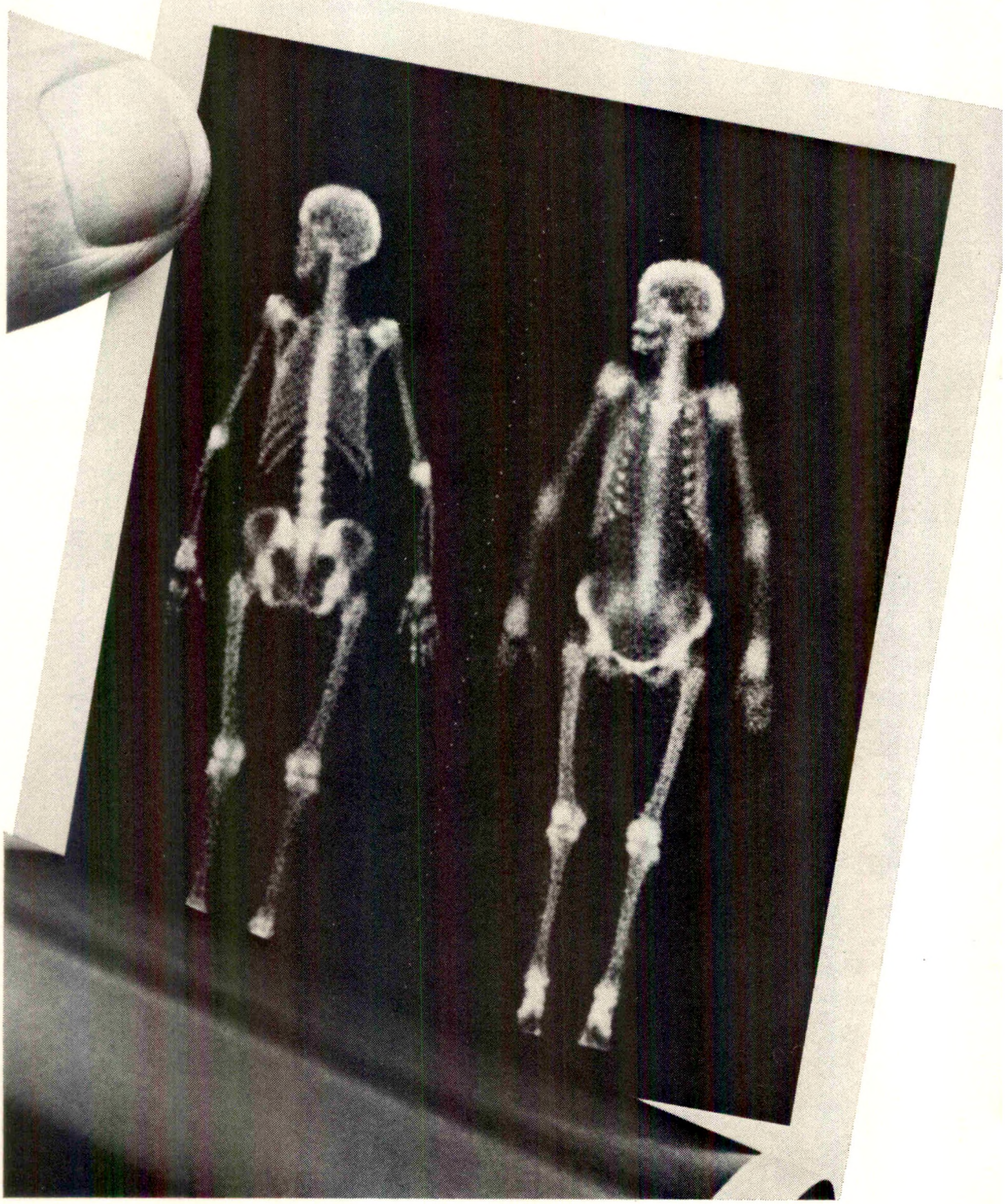

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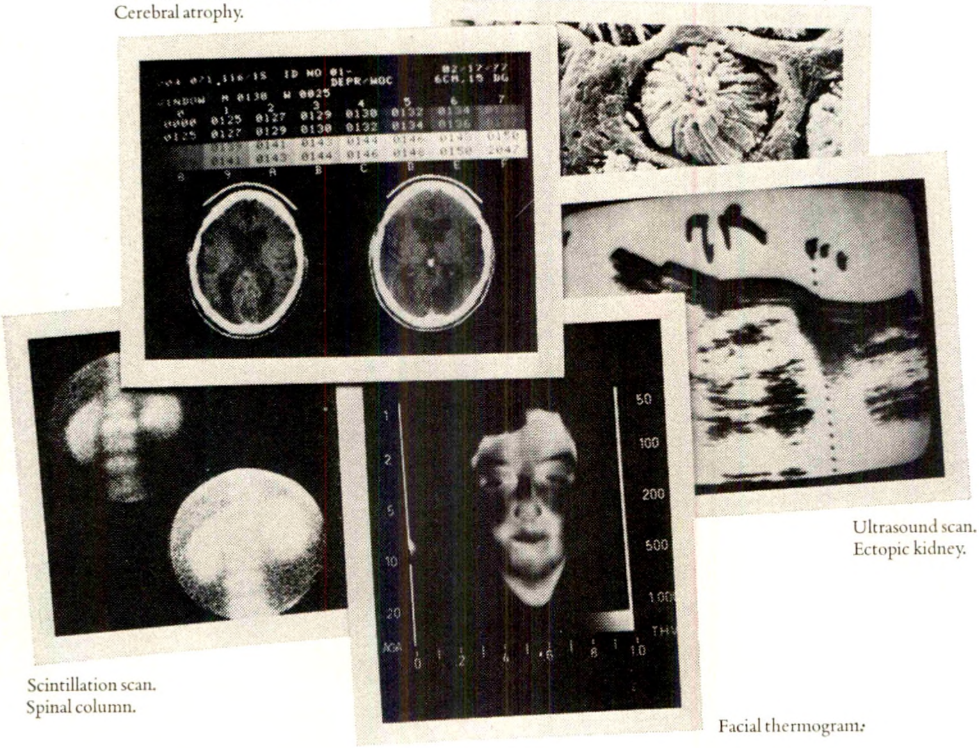

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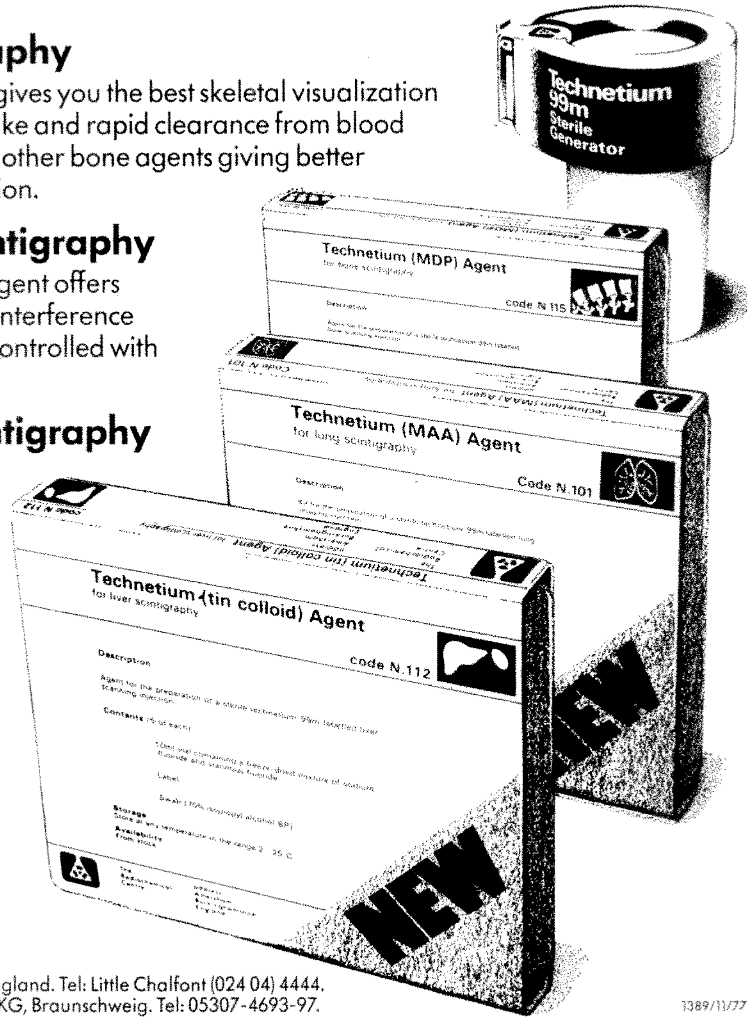

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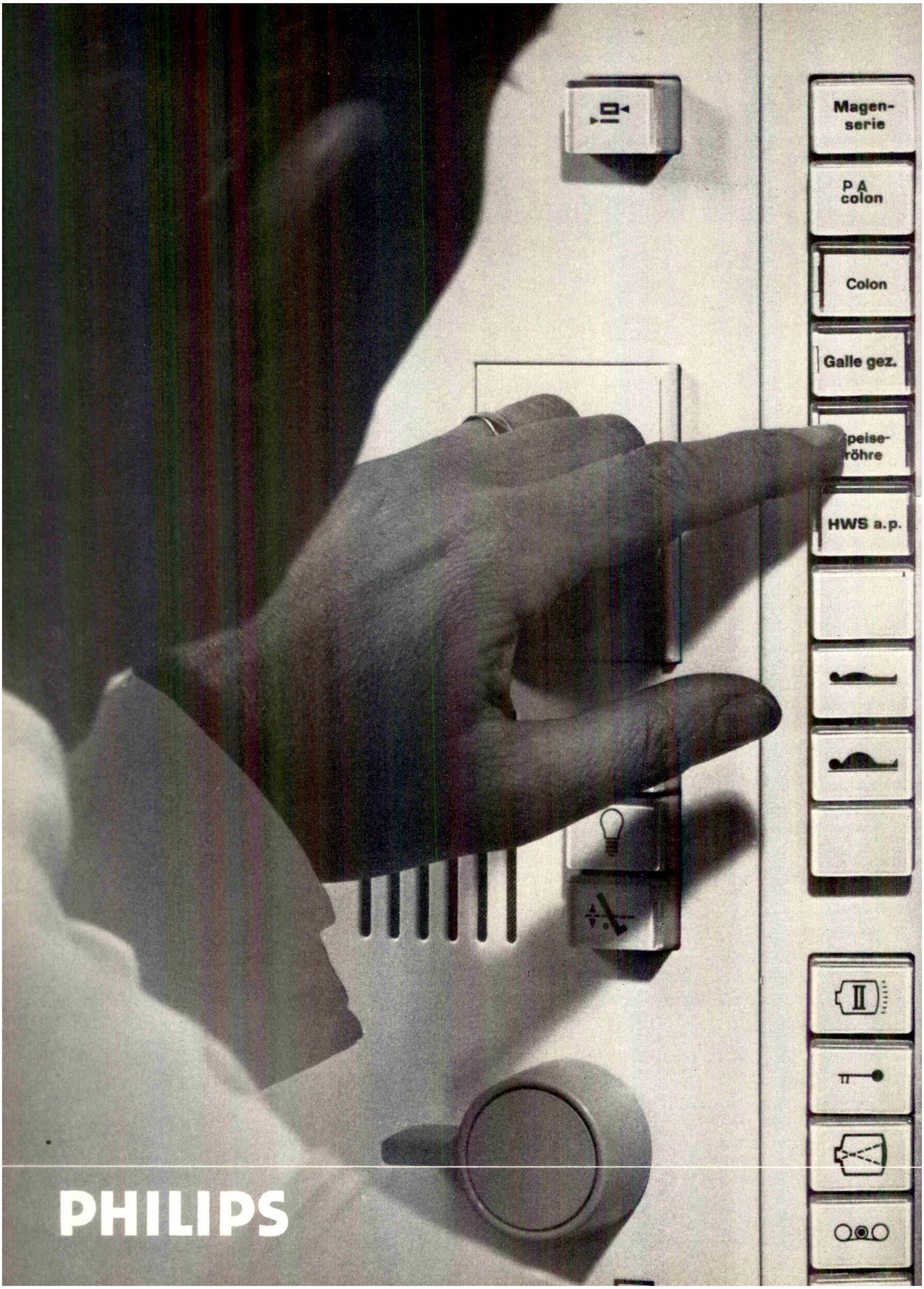
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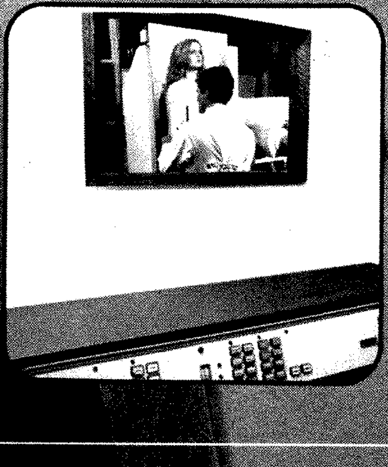

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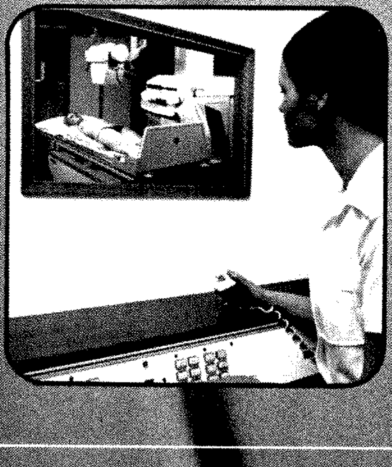

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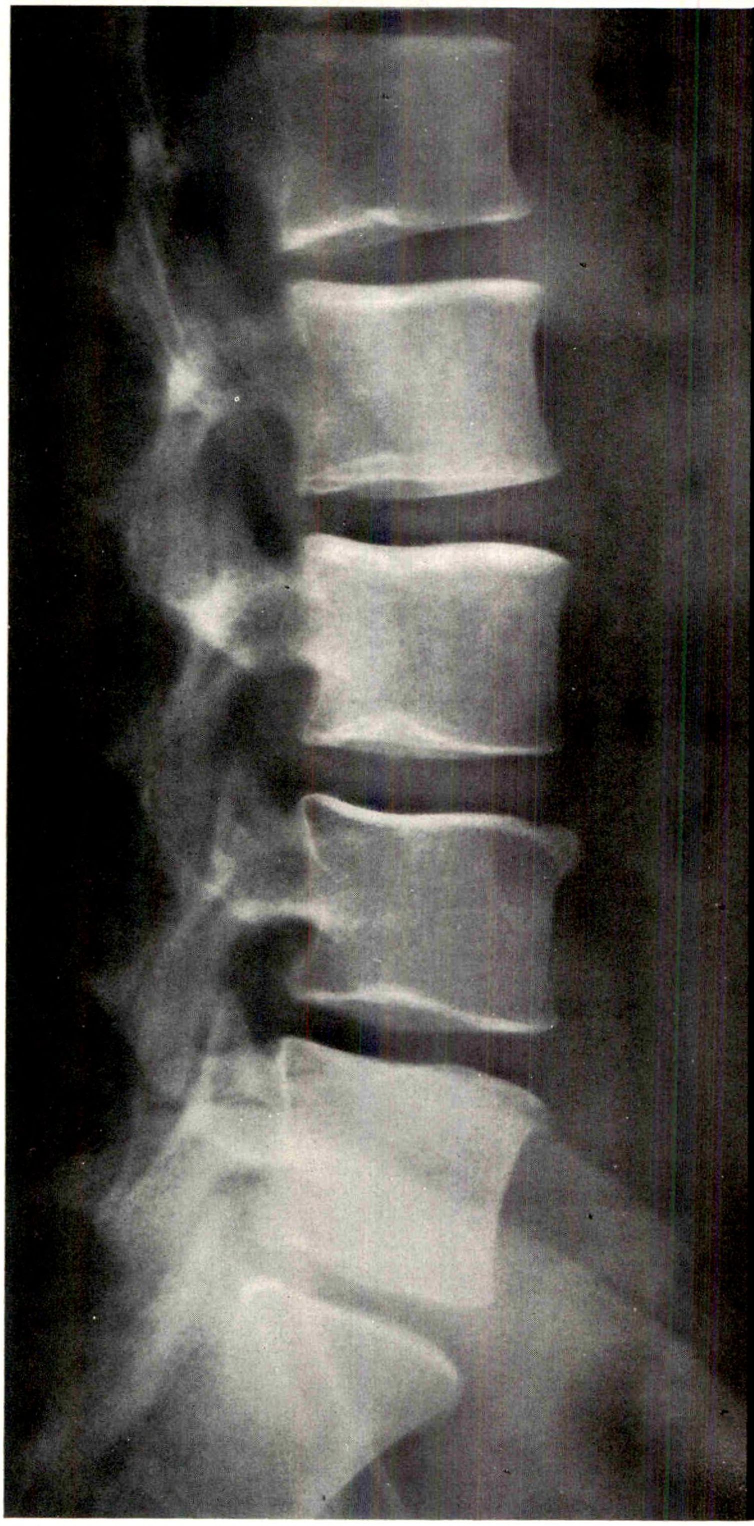

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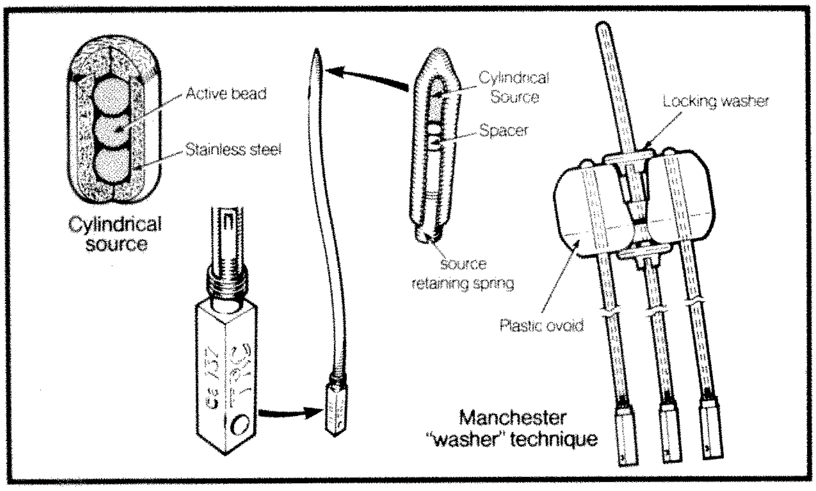

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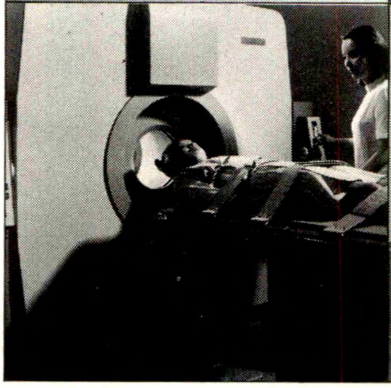

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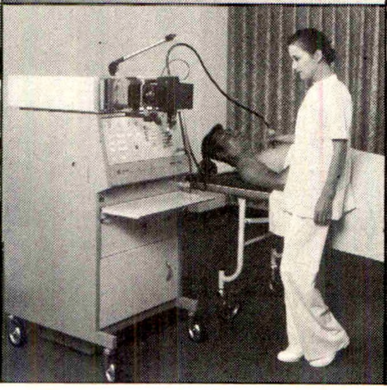

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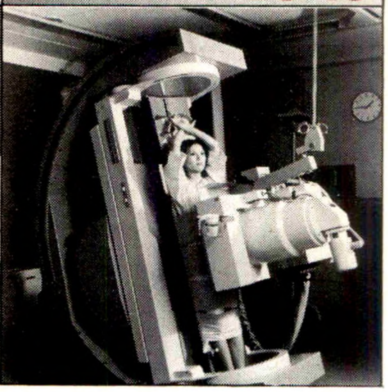

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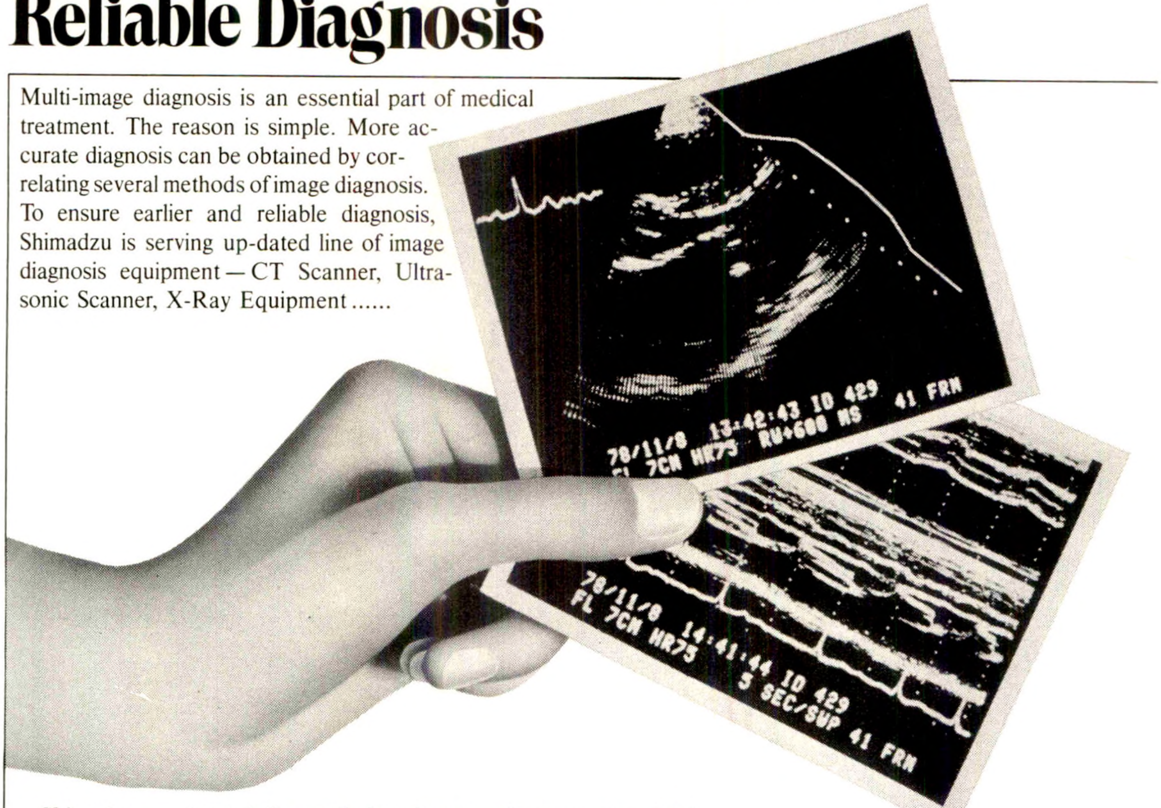

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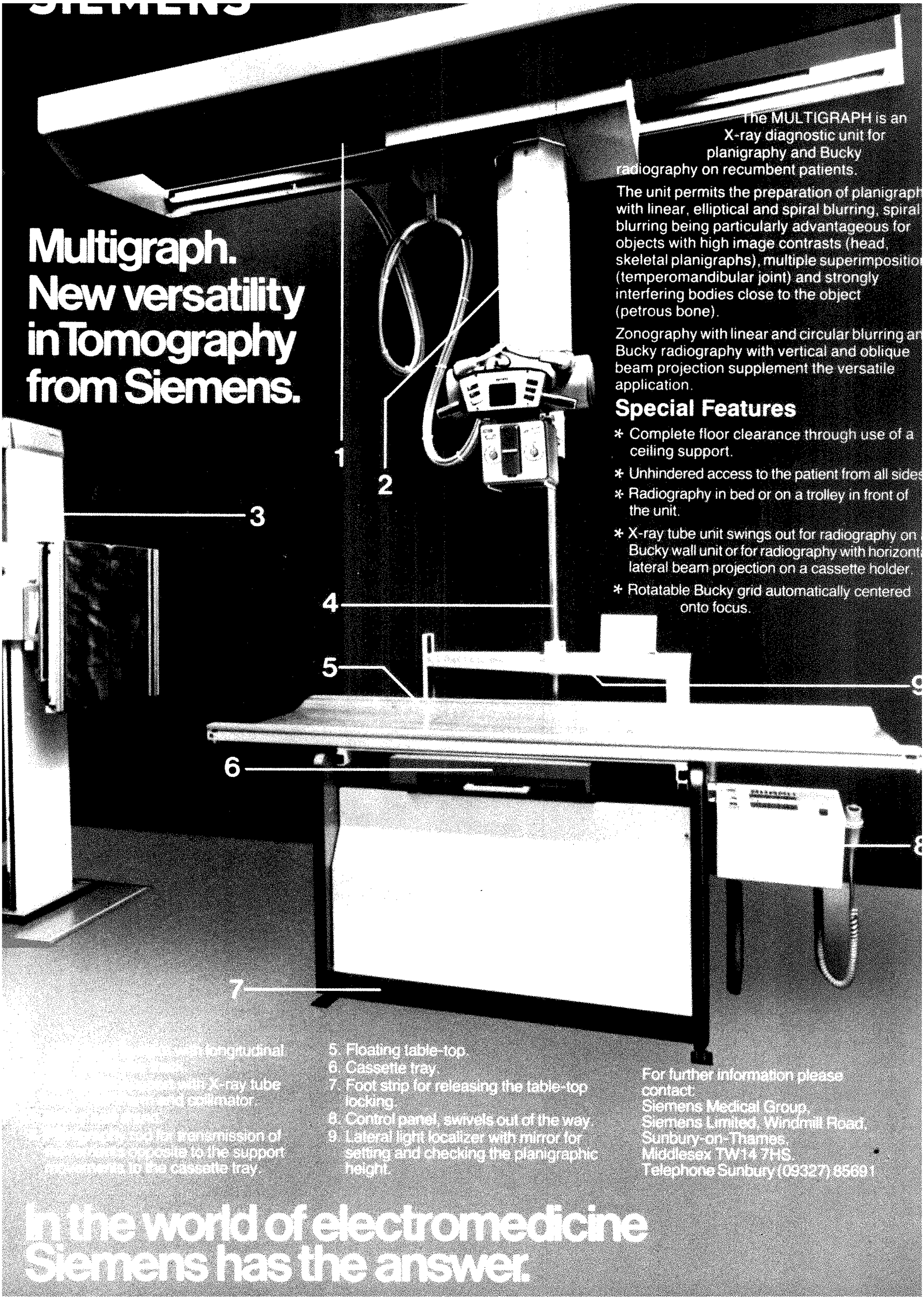

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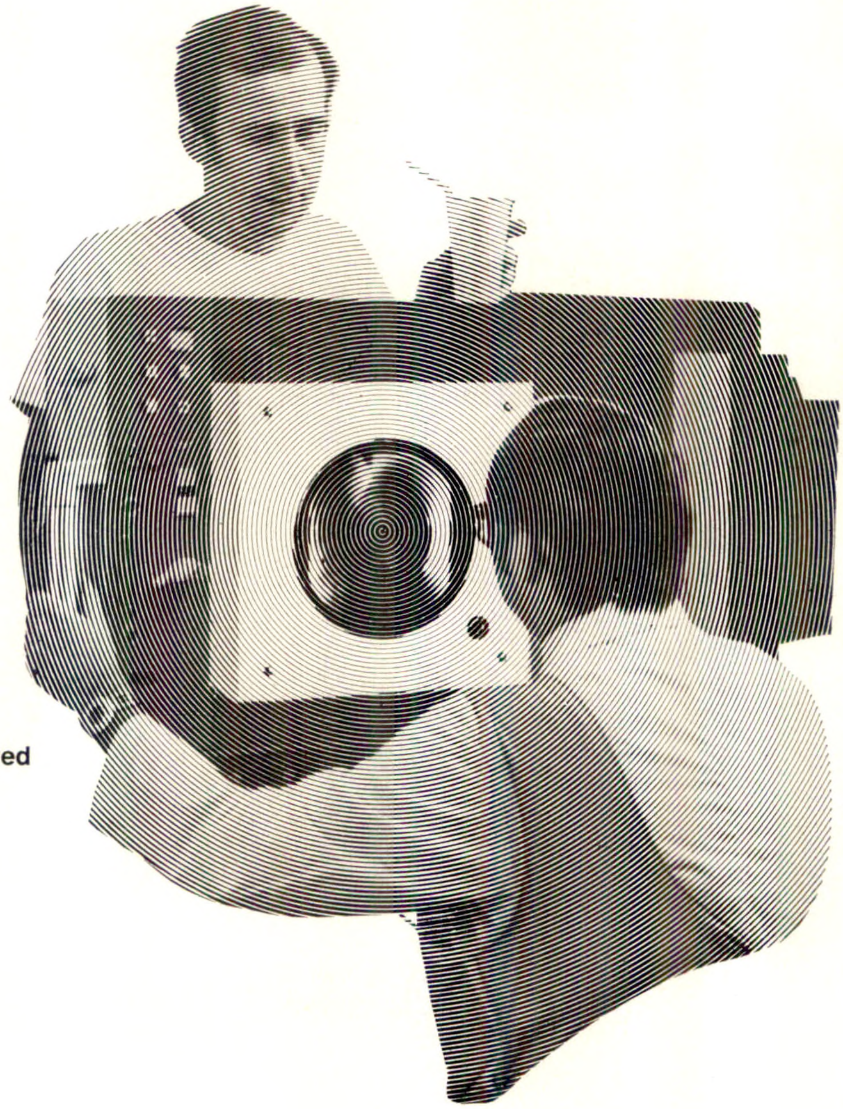

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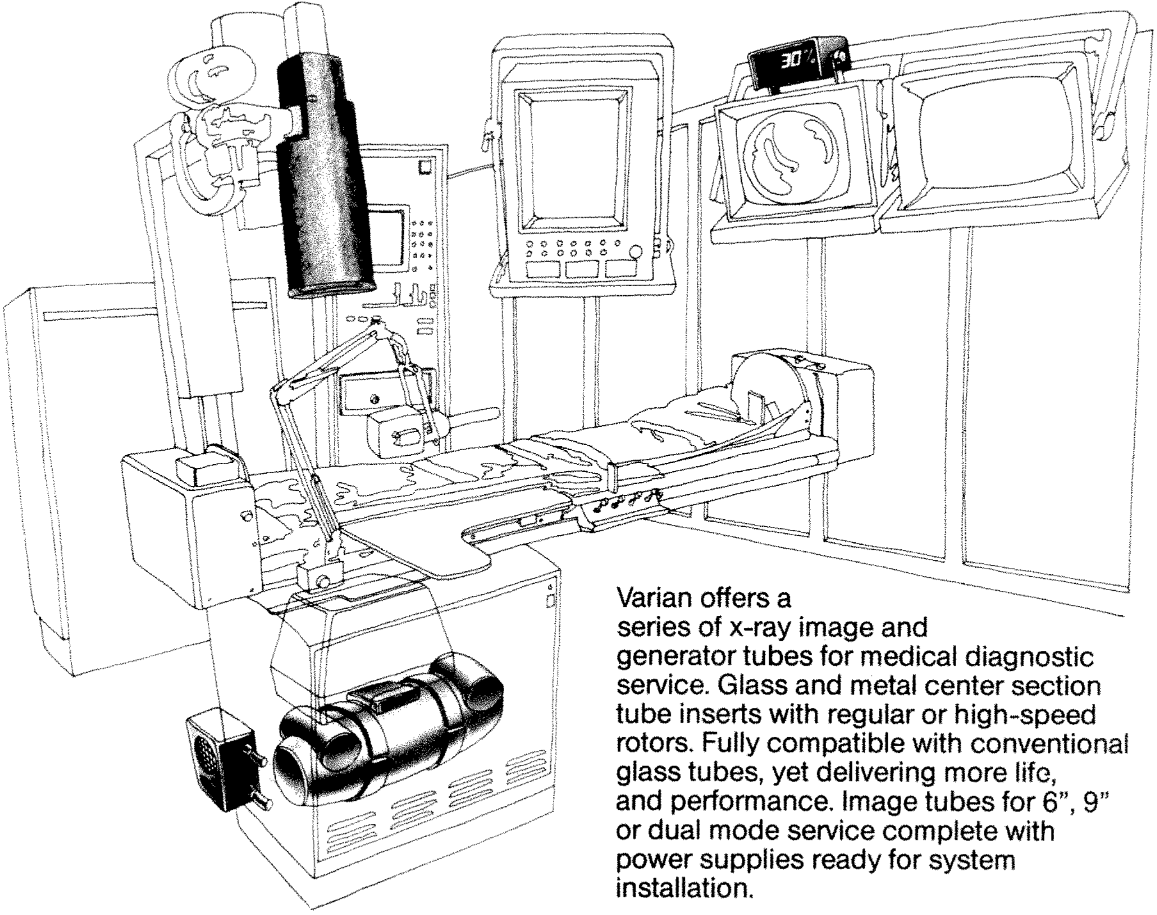

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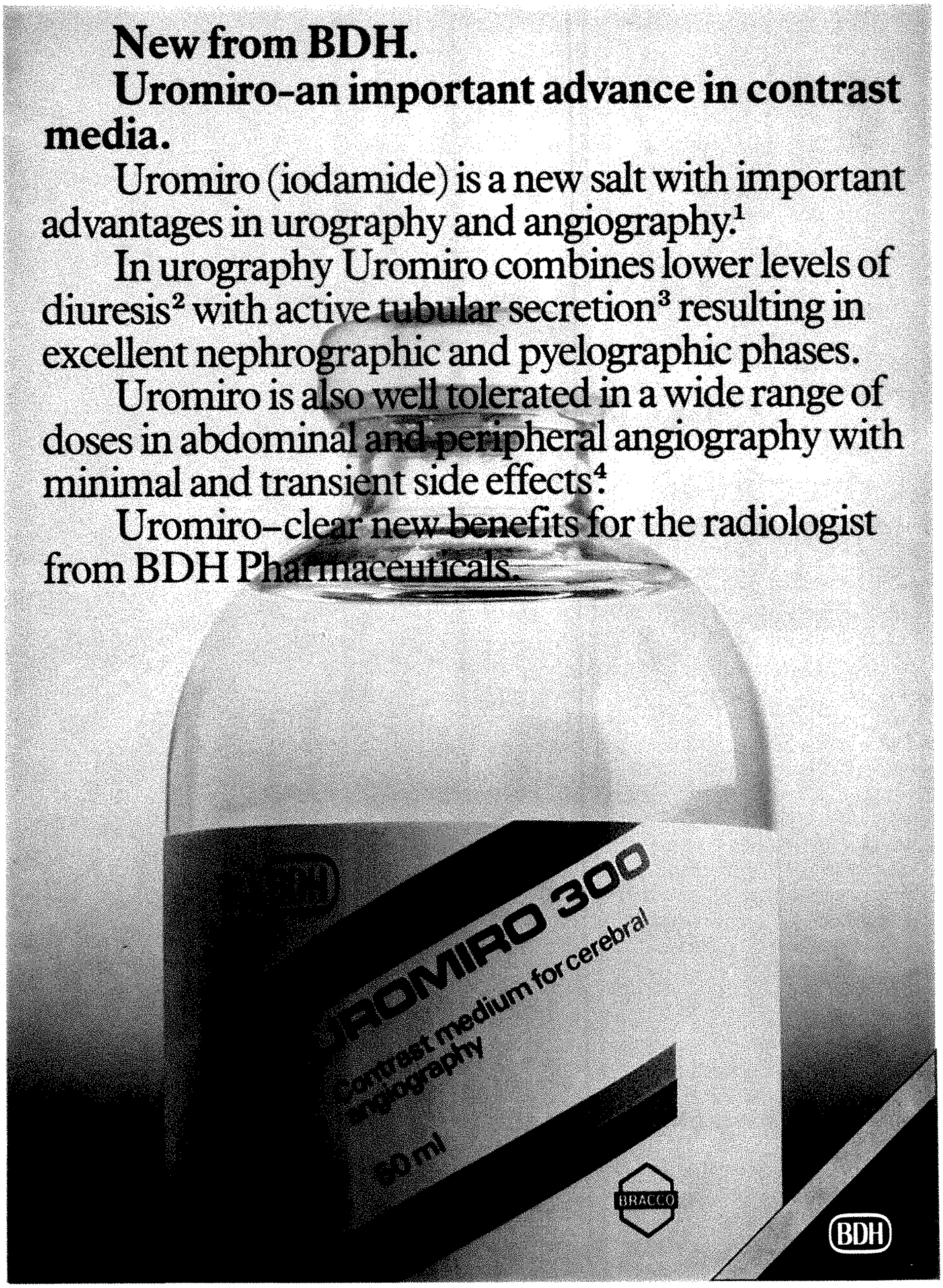

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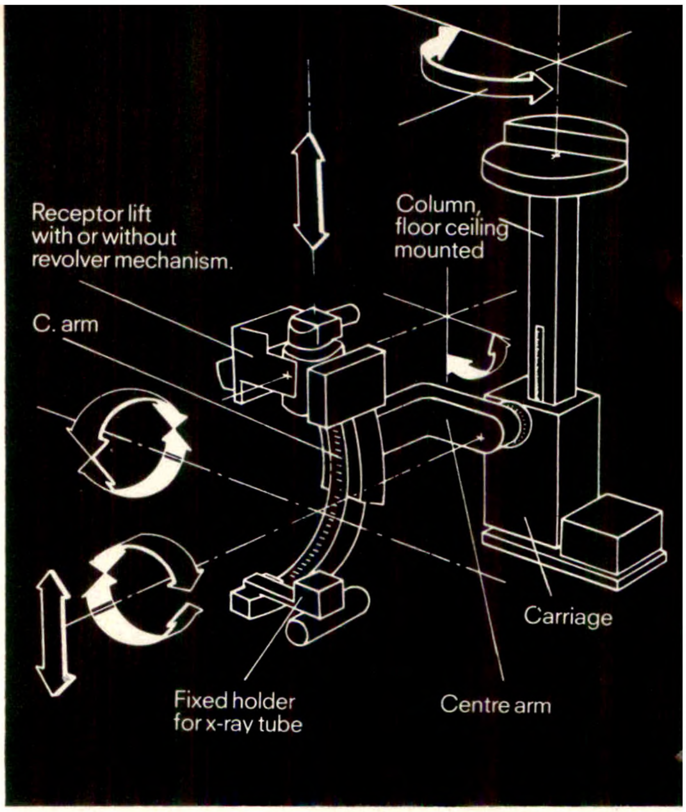

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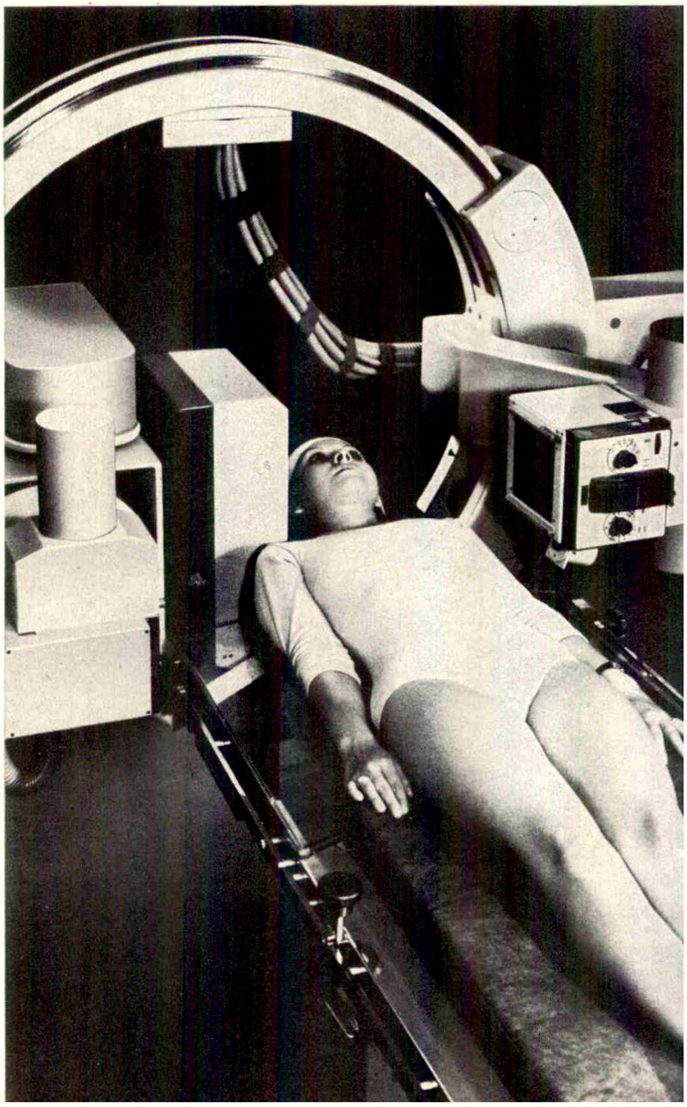

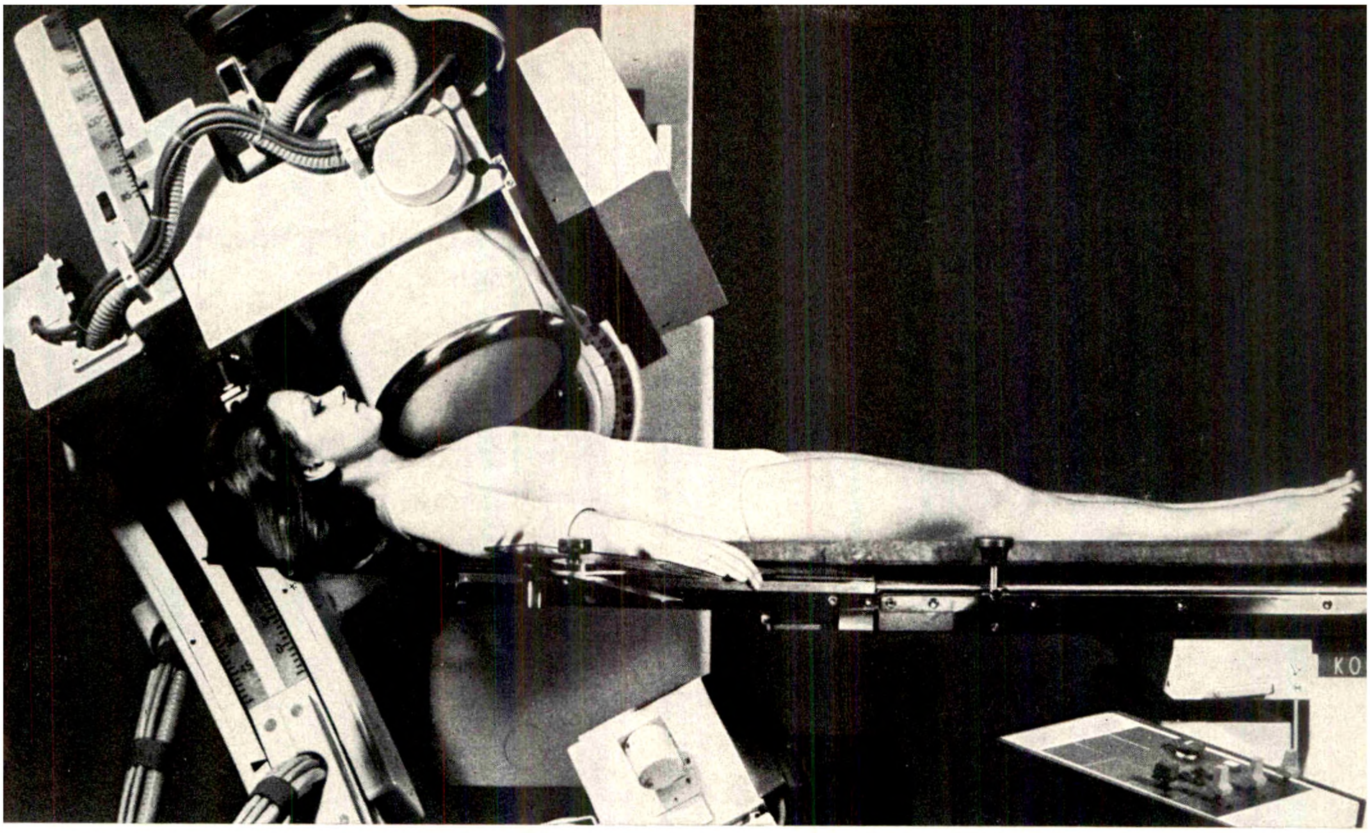

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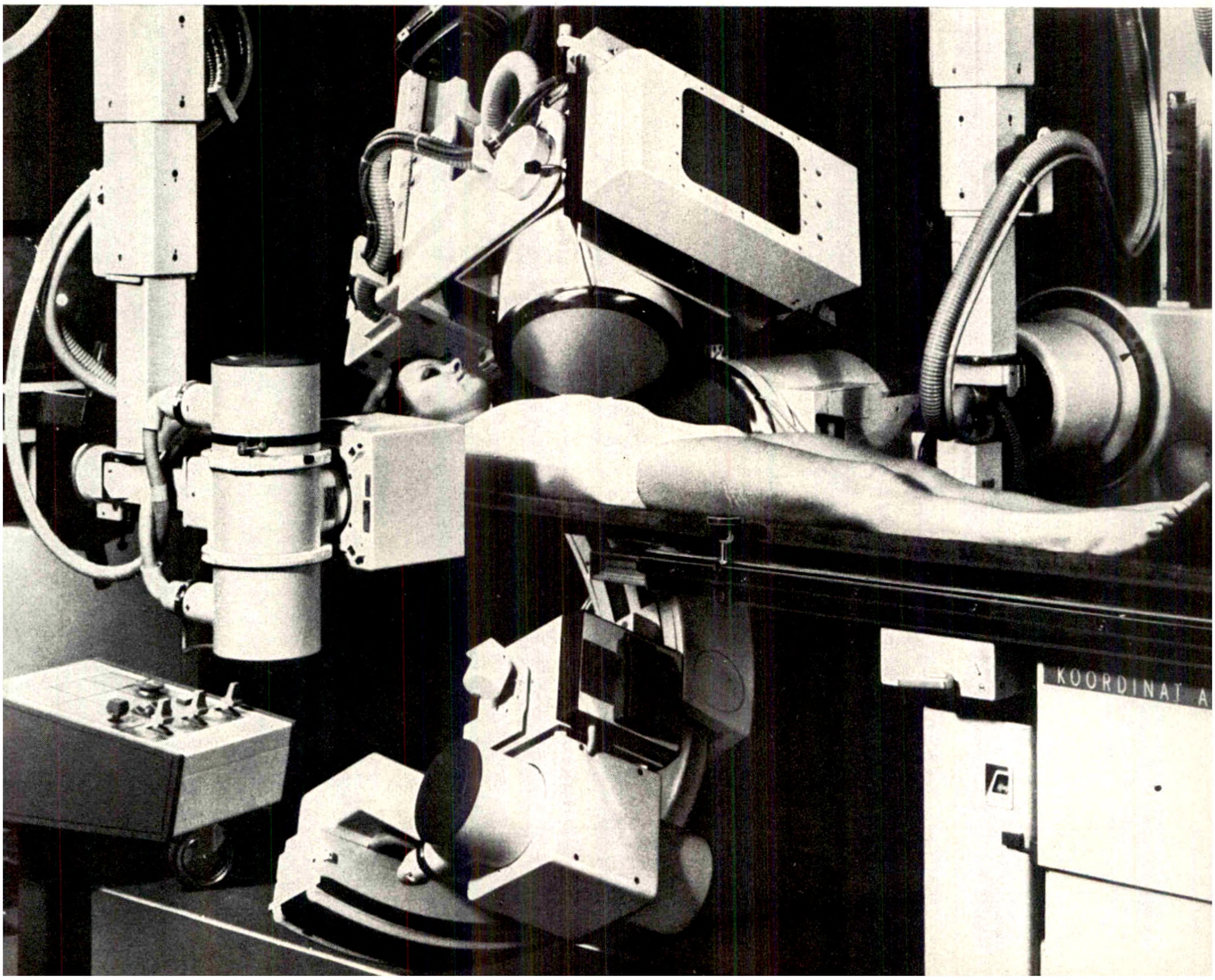

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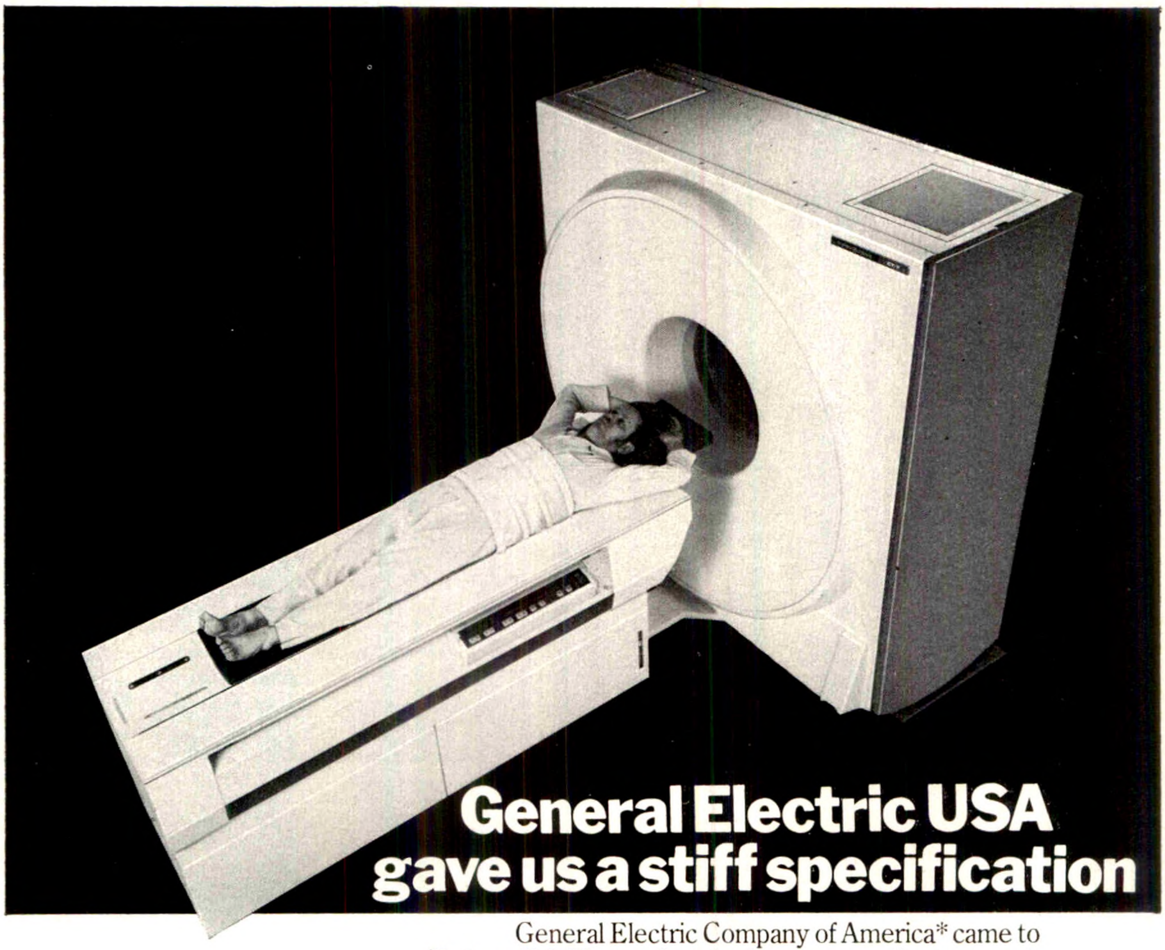

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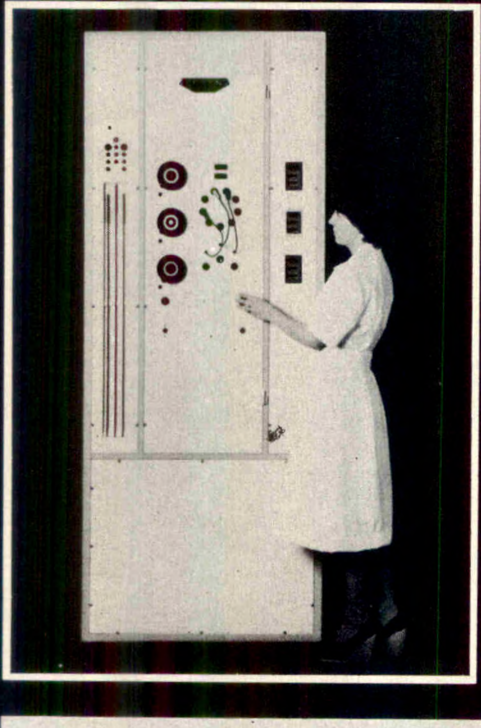

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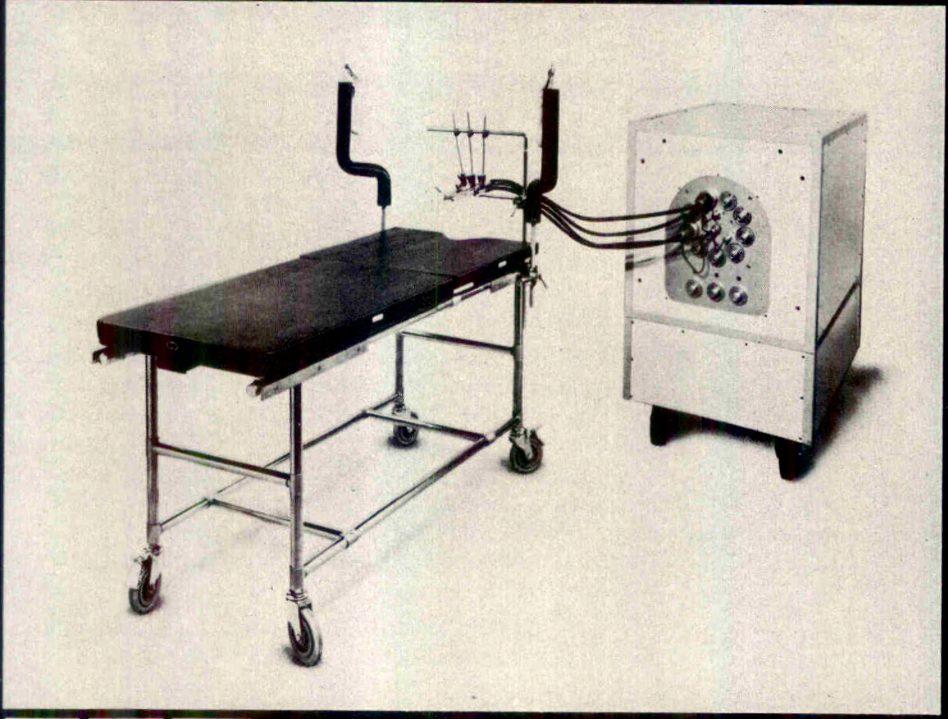

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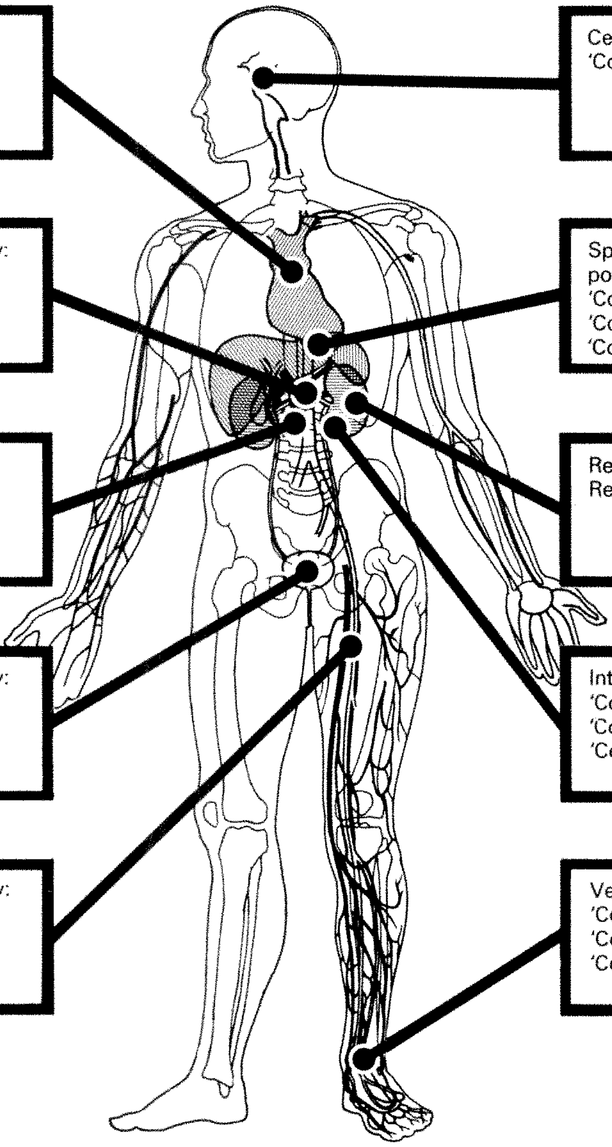

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11.50	Isotope imaging in cardiology	Duncan Dymond
12.30	Discussion	
2.15	Radiology of heart failure	Basil Strickland
2.35	Lung scanning and pulmonary embolism	Peter Ell
2.55	The postoperative X-ray	Margaret Branthwaite
3.15	Discussion	
3.30	Film quiz	

Thursday 14th June

9.30	Clinical presentation of congenital heart disease	Jane Somerville
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11.20	Radiological differential diagnosis in the cyanosed patient	Basil Strickland
11.40	Radiology of continuous murmers	Simon Rees
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2.00	Left ventricular function in ischaemic heart disease	Derek Gibson
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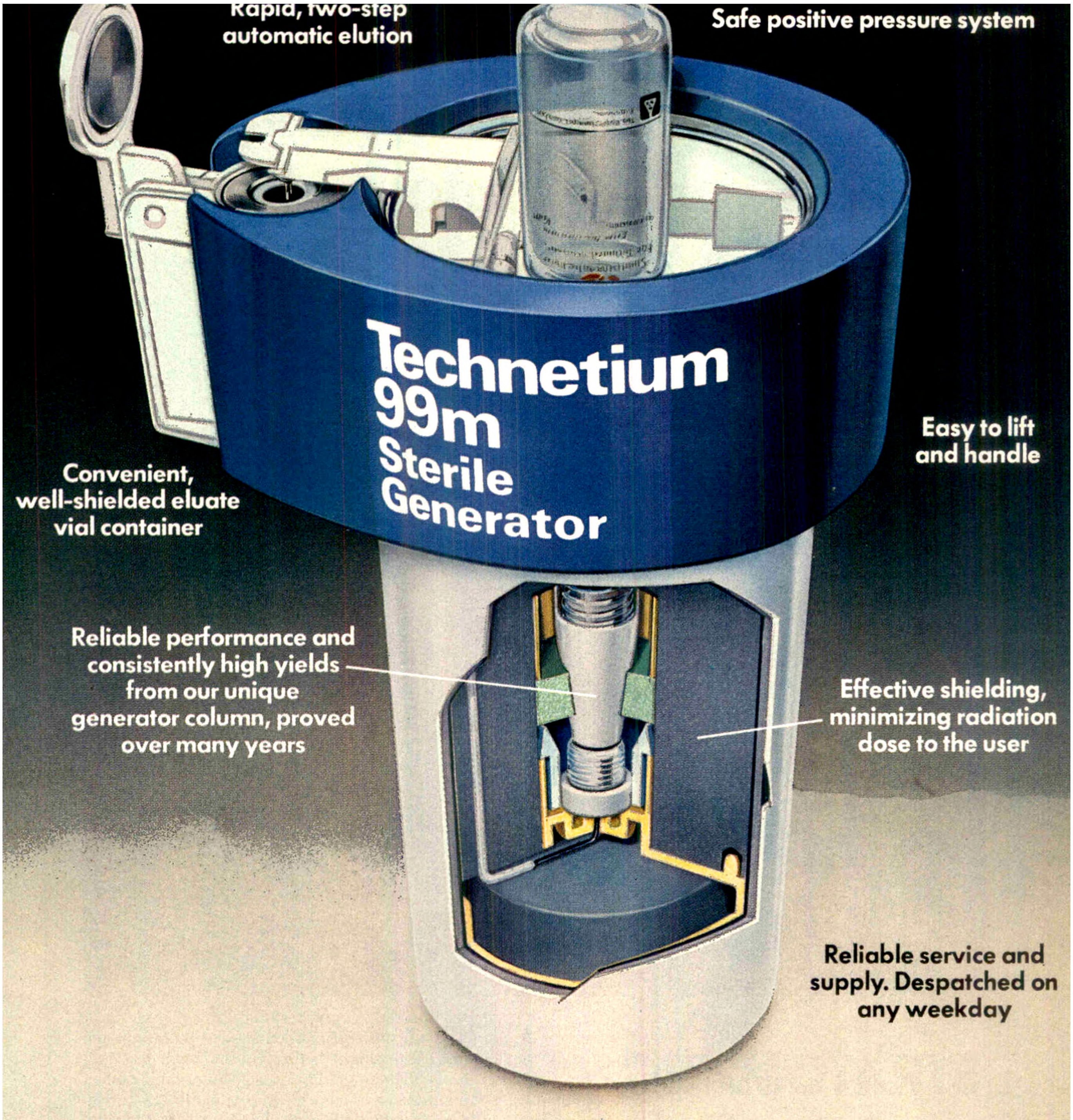
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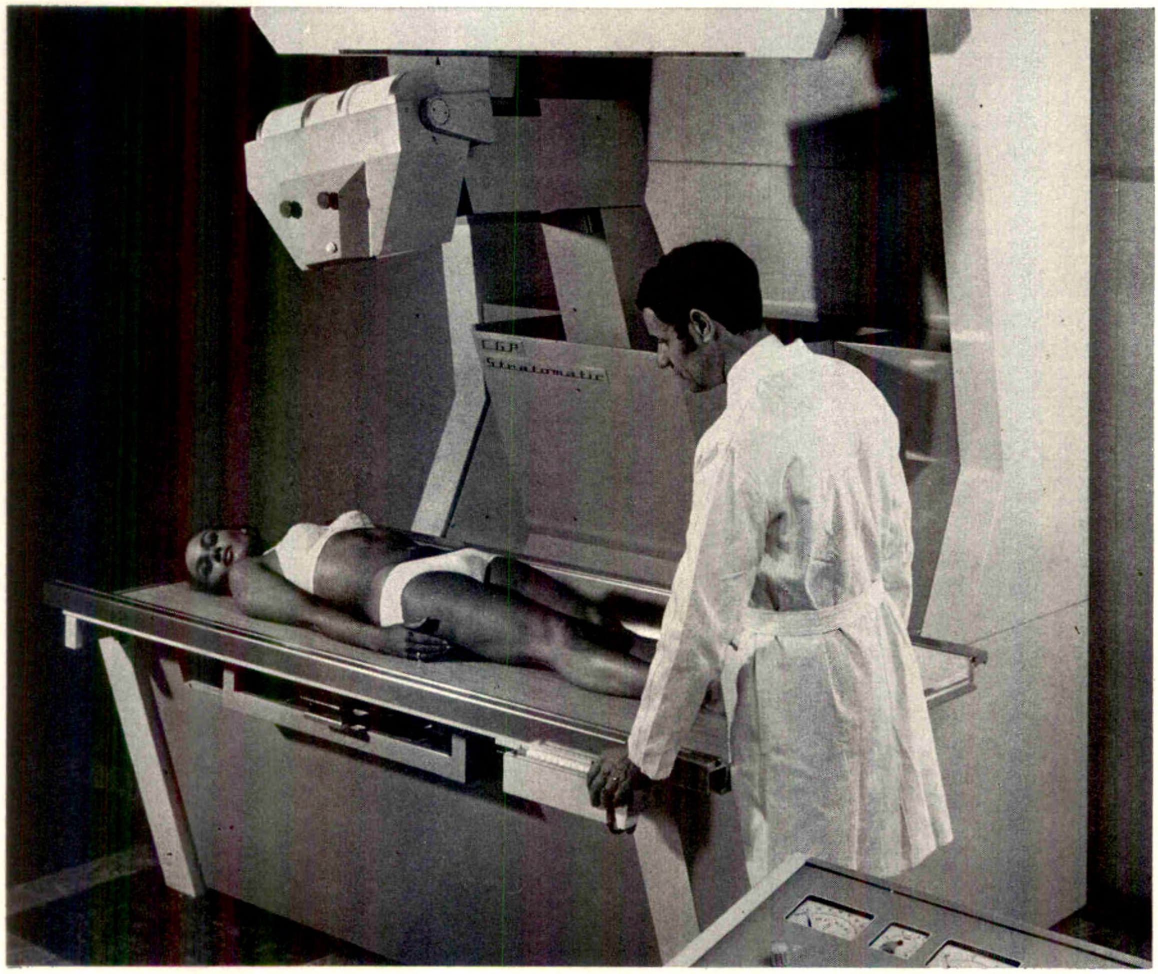

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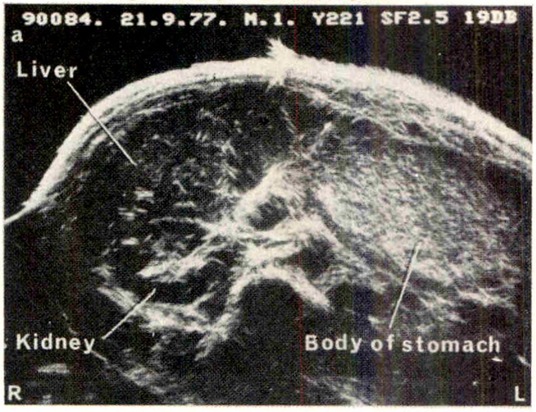

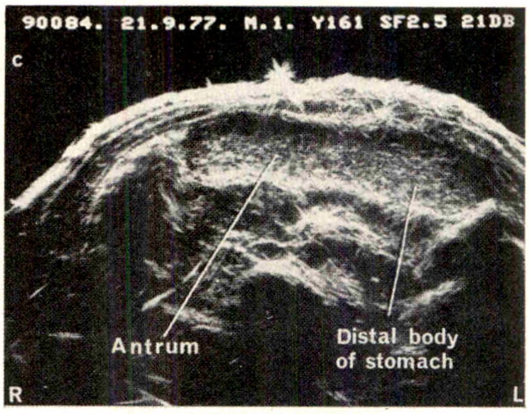

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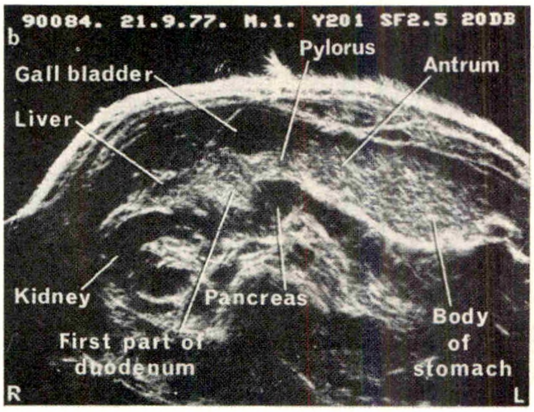

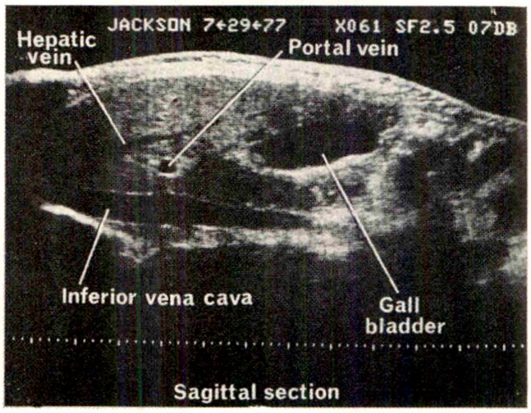

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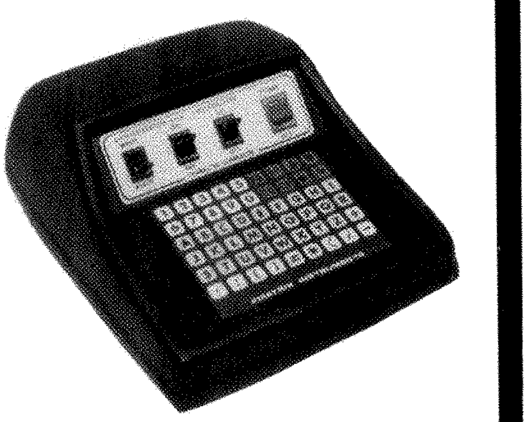

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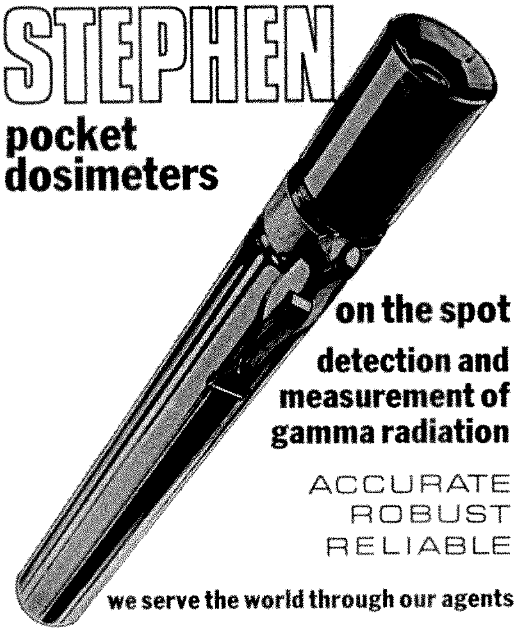

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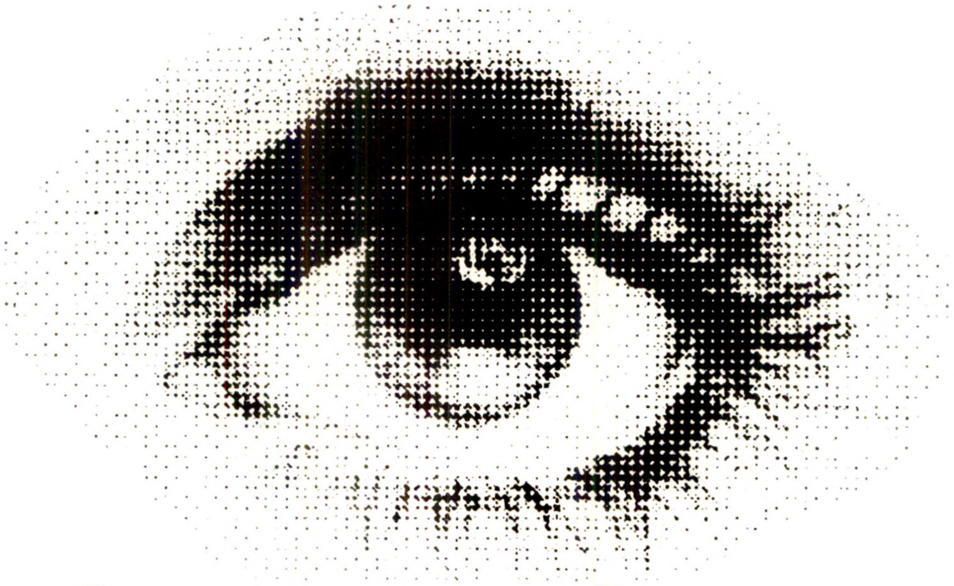

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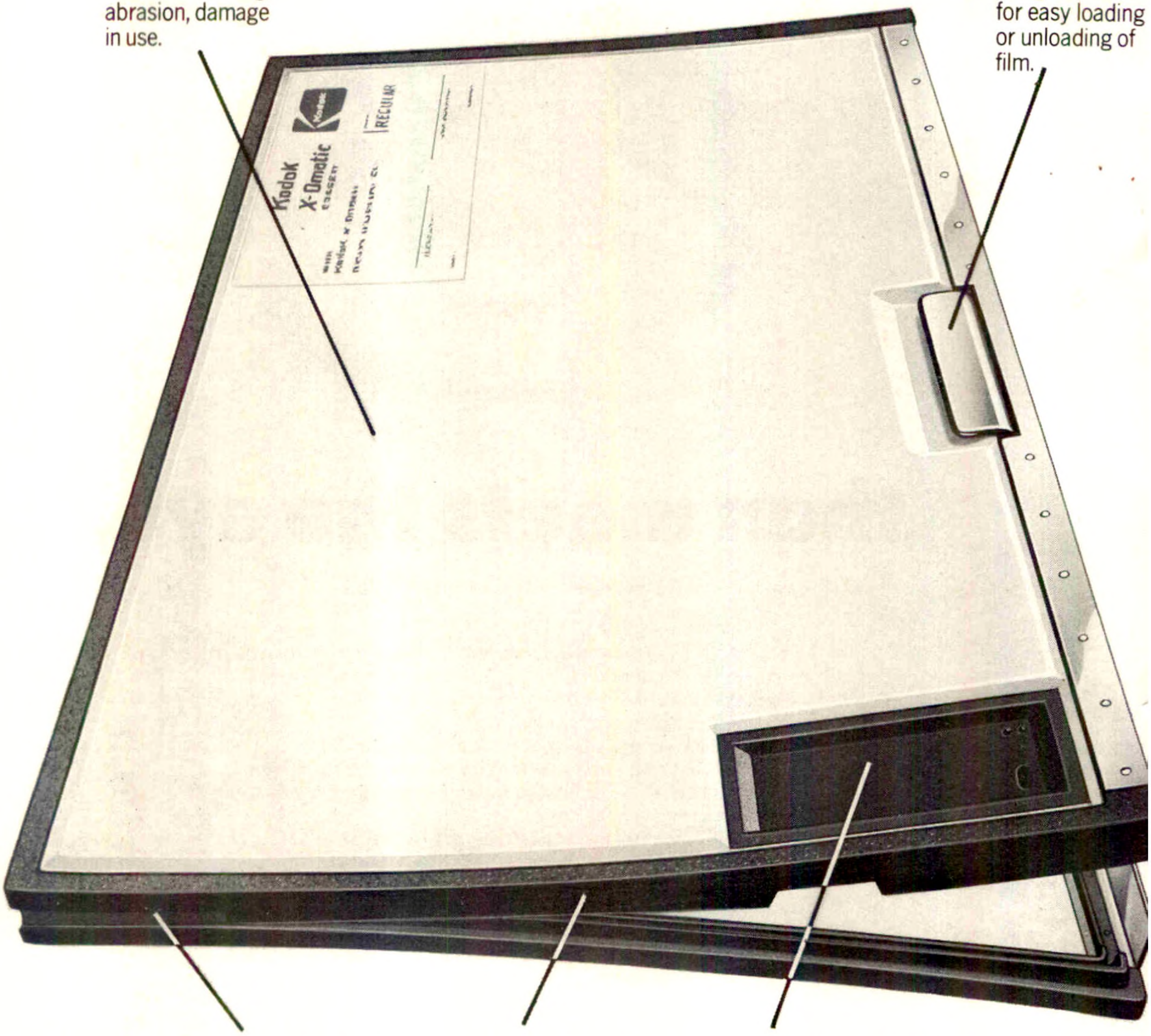

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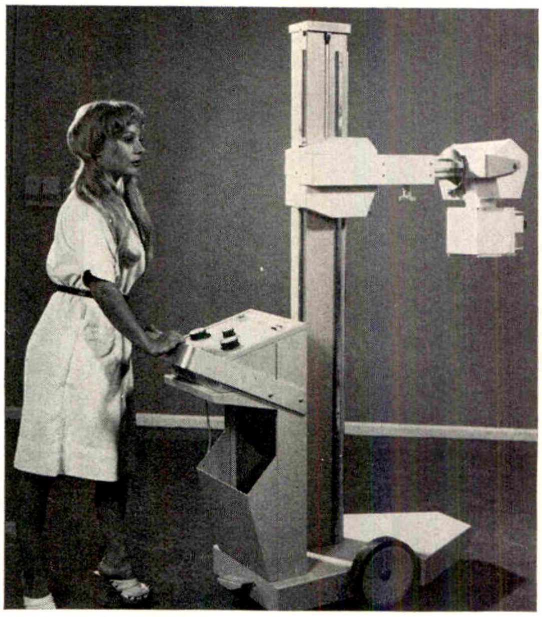

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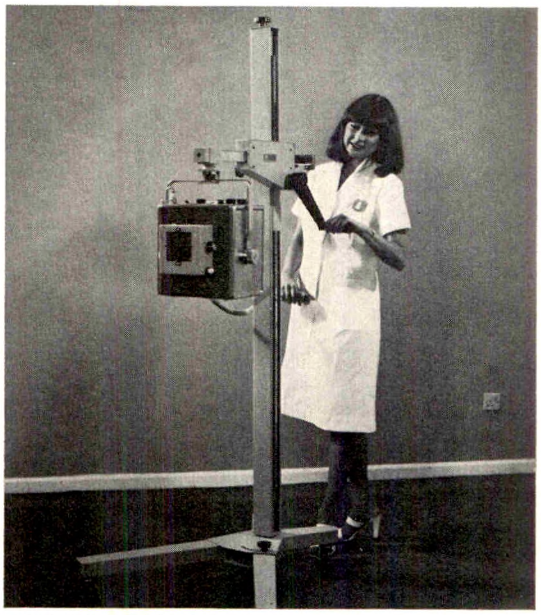

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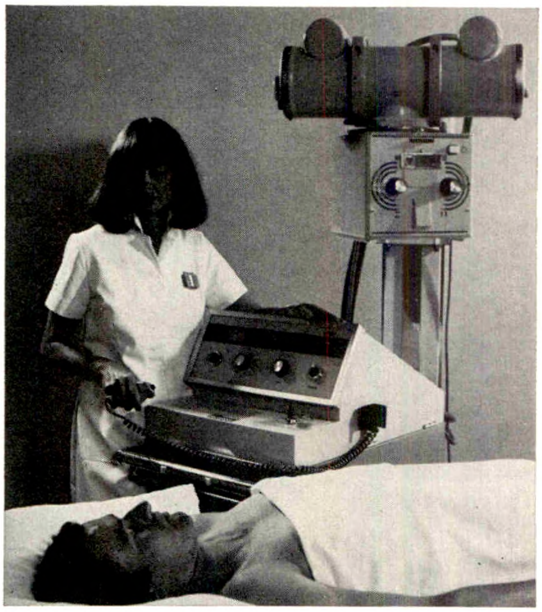

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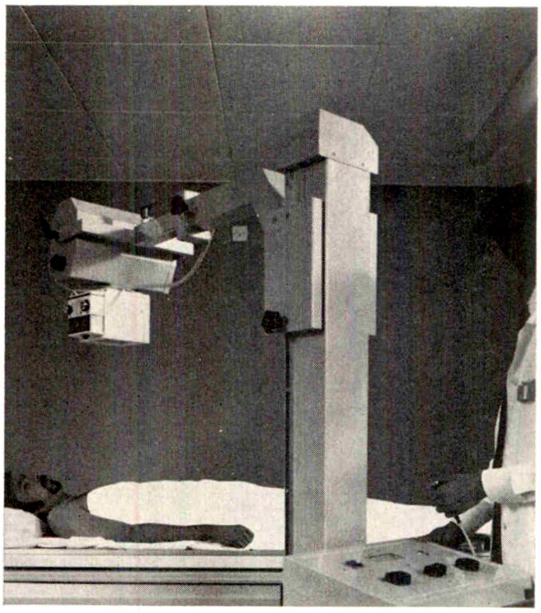

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The British Journal of Radiology

Review article

Short-life radionuclides and regional lung function

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1. INTRODUCTION

Short-life γ-emitting radionuclides are particularly suitable for studies of the function of different regions of the lung. All the important constituents of the gas in the lungs (oxygen, carbon dioxide and nitrogen) can be labelled with these isotopes. Their distribution can be sensed by detectors placed externally so that the procedures are non-invasive. Because of their short physical half-lives (less than 20 min), cyclotron-produced gaseous isotopes give little radiation exposure.

The healthy lung achieves its function, the exchange of oxygen and carbon dioxide, by maintaining an approximately equal flow of air and blood into each of the 300 million air sacs or alveoli. For each unit, the ratio of alveolar ventilation ($\dot{V}_A$) to blood flow ($\dot{Q}$), the $\dot{V}_A/\dot{Q}$ ratio, approaches unity. Nearly all cases of hypoxaemia (low arterial PO_2, breathing air) are associated with a wide dispersion of $\dot{V}_A/\dot{Q}$ ratios through the lung. This can be studied in two ways using short-life radionuclides: (1) the distribution of oxygen (as ^{15}O) or carbon dioxide ($^{11}CO_2$) can be monitored because the concentration of either gas in any lung unit is determined by the local $\dot{V}_A/\dot{Q}$ ratio, or (2) alveolar ventilation ($\dot{V}_A$) or blood flow ($\dot{Q}$) can be measured separately using $C^{15}O_2$ or inert gases such as ^{13}N or $^{81}Kr^m$. The second approach is generally used in practice.

While measurements of the distribution of ventilation and perfusion are not needed to assess the efficiency of the lung (there are simpler methods such as blood-gas analysis and routine pulmonary function tests) they may indicate whether it is ventilation or perfusion which is the most affected. For example, the hypoxaemia and dyspnoea associated with pulmonary embolism (uneven distribution of perfusion with an even pattern of ventilation) demands different treatment from that seen in asthma, for example, where the abnormalities of distribution are predominantly ventilatory.

Even in normal lungs there are inequalities betweeen local ventilation and perfusion; these are mainly related to gravity. The lung and the chest

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wall (including the diaphragm) are relatively compliant and fairly easily deformed by their own weight and that of the heart and abdomen; this is particularly obvious when posture is changed (Amis *et al.*, 1977) or when the diaphragm is paralysed. In addition, the low pulmonary arterial pressure in relation to the height of the lung makes the distribution of blood flow in an organ as large as the lung extremely gravity-dependent. Thus, the topography of ventilation and perfusion holds as much interest for the physiologist as for the clinician. For the radiologist, lung scans giving functional information about flow distributions may be an important adjunct to the anatomical information about structure provided by the chest radiograph.

Topographical measurements with radionuclides have their limitations. For example, the distribution of radioactivity in the lung recorded with a gamma camera placed behind the subject is a two dimensional representation of a three dimensional structure. Even if anterior and lateral views are used, considerable distortion is introduced because of attenuation of the signal from deeper parts of the lung. Attenuation also depends on the density of the lung, the thickness of the chest wall and the γ-ray energy of the isotope. From front to back of an inflated lung 10 cm thick there is a 45% fall in counting efficiency for ^{133}Xe (80 keV) but only 28% for positron emitters such as ^{13}N (511 keV). Secondly, there are limitations imposed by the spatial resolution of the detecting devices. Maldistribution of ventilation and perfusion between respiratory units less than 1.5–2.0 cm diameter cannot be resolved with any accuracy, but $\dot{V}_A/\dot{Q}$ mismatching on a microscopic level is as frequent as that on a macroscopic scale. Finally, there is the problem, shared with conventional radiology, of overlapping of units with different function in the same counting field. Tomographic devices are being developed in an effort to overcome this problem but they will be very expensive.

1.1 *Historical*

The first cyclotron on a hospital site was built for the Medical Research Council and was commissioned at Hammersmith Hospital in 1956. Much of the early clinical and physiological investigations were carried out on the lung using molecular ^{15}O and oxygen-labelled compounds such as $C^{15}O_2$, $C^{15}O$ and $H_2{}^{15}O$. The work of Dollery, Dyson, Hugh-Jones, Matthews and West on the lung between 1958 and 1962 became very well known. This early work is summarized in a recent book by J. B. West (1977) and I shall not describe it in any detail.

TABLE I

Use of short-life radioisotopes for measurements of regional lung function

Isotope	$t_{\frac{1}{2}}$	γ-energy (keV)	Measurements
^{81}Kr^m	13 sec	190	Ventilation, blood flow
$C^{15}O_2$	2.1 min	511	Blood flow, lung water
$H_2{}^{15}O$	2.1 min	511	Lung water
$C^{15}O$	2.1 min	511	Tissue diffusion, lung haemorrhage
^{13}N	10 min	511	Ventilation, blood flow, volume, ventilation-perfusion ratio
^{11}CO-red cells	20 min	511	Pulmonary blood volume and flow

1.2 *Available isotopes*

The principle short-life radionuclides in use now are listed in Table I. For obvious reasons, use of these nuclides is restricted to a few hospitals and centres in the vicinity of a cyclotron. Thus, for clinical measurements most investigators have turned to radionuclides with a much longer half-life, such as ^{133}Xe or ^{99}Tc^m. Nevertheless, for cyclotron users, the main constituents of the dry gas fraction in the lung (oxygen, carbon dioxide and nitrogen) all have γ-emitting isotopes (^{15}O, $C^{15}O_2$ or $^{11}CO_2$, ^{13}N) which are readily available. They belong to a class of radionuclides called positron-emitters. When a positron combines with an electron in tissue, two photons are given off at 180 deg to each other. Since the photon emission for all positrons is a pair of 511 keV γ-rays, ^{13}N, ^{11}C, and ^{15}O can be counted under identical geometric conditions. Thus Jones *et al.* (1975) could compare distributions of blood flow (^{13}N), blood volume (^{11}CO labelled red cells), lung water ($H_2{}^{15}O$) and gas volume (^{13}N) under similar counting conditions. Using a pair of detectors facing each other, positron emission can be detected by coincidence counting in which the disintegrations are located within the cylinder formed by the two opposed counters. With two banks of counters facing each other, used in coincidence to produce a positron camera, the distribution of radioactivity in two dimensions can be recorded at different depths without heavy shielding. The application of tomography to radioisotopic measurements of regional lung function is eagerly awaited; preliminary measurements from Massachusetts General Hospital using a positron camera have been reported (Chesler *et al.*, 1975) and work at Hammersmith is just beginning.

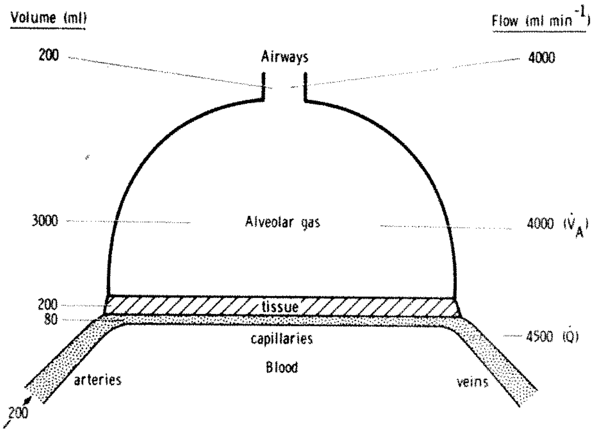

FIG. 1.

Schematic diagram of the lung showing volumes and flows in the airway, alveolar, tissue and blood compartments.

An interesting development in recent years has been $^{81}Kr^m$ (half life 13 sec) given by continuous inhalation or infusion to measure ventilation and perfusion distribution. Krypton-81m has several clinical applications, many of which were discussed at an International Meeting devoted to this isotope (Lavender, 1978). Immediate access to a cyclotron is not necessary because $^{81}Kr^m$ can be generated continuously from its parent ^{81}Rb which has a 4.58 hour half-life. The positron emitters (^{13}N, ^{15}O) can only be used locally. Details about the production of these short-lived radioactive gases are given in an excellent book by Clark and Buckingham (1975).

2. THEORY AND METHODS

2.1 *Nature of the lung*

It may help to review a few facts about lung structure and function (Fig. 1). Basically, the lung consists of airways which conduct gas into the alveolar compartment where O_2 and CO_2 diffuse into and out of pulmonary capillary blood, a tissue skeleton, and an extensive network of blood vessels. Most of the volume is contained in the alveolar compartment. The capillary volume is small (80 ml) but increases 2–3 times on exercise. The volume of blood in the arteries and veins is about 400 ml. The important physiological indices are flow per unit volume and $\dot{V}_A/\dot{Q}$. Alveolar ventilation per unit volume is 1.33 min^{-1} (4000/3000), about one-twentieth of the turnover of the dead space (27 min^{-1}) and one-fortieth of the turnover of capillary volume (56 min^{-1}). The average time spent by a red cell in the capillary bed is less than one second. This is more than sufficient for the red cells to be fully saturated with oxygen because the diffusion distances from alveolar gas to red cell are short ($< 1 \mu m$) and the rate of combination of oxygen with haemoglobin is rapid. The $\dot{V}_A/\dot{Q}$ ratio, together with the composition of pulmonary arterial blood and inspired gas, determines the oxygen and CO_2 tensions of each individual respiratory unit. A uniformly perfused and ventilated lung with a $\dot{V}_A/\dot{Q}$ ratio of 0.88 (4000/4500) would have an alveolar PO_2 and PCO_2 of 100 and 40 mmHg respectively, and the haemoglobin of the venous blood leaving the lung would be 97% saturated with oxygen.

Figure 1 considers the lung as a single compartment rather than as 300×10^6 separate units; nevertheless, the principles remain the same, even though the individual values for flow/unit volume and $\dot{V}_A/\dot{Q}$ may show considerable dispersion around the mean. Inhomogeneities of ventilation are generally described as being in parallel or in series. Parallel differences exist between units and series differences refer to gradients of concentration from proximal to distal within a single unit.

2.2 *Measurement of ventilation distribution*

There are two main methods for recording regional ventilation. In the first, the subject takes a tidal breath of an insoluble marker gas, such as ^{13}N or ^{133}Xe, and holds his breath while count rates are recorded over the chest. If a gas with ultra-short half-life such as $^{81}Kr^m$ is used, a series of single breaths can be taken in succession without a pause and a similar result achieved (see section 4.1). Following the single breath, the count rate reflects flow and not flow per unit volume. Thus, it is influenced by geometric factors such as attenuation and the volume of lung in the counting field. A second measurement is usually made after equilibrating the subject with the marker gas in closed circuit. If the concentration of isotope is the same in all lung units, the local count rate will be proportional to volume. Dividing the ventilation by the volume image takes into account these geometric factors including attenuation, providing both measurements are made at the same overall lung volume.

A second method of measuring ventilation is to record the wash-in or wash-out of the marker gas. Following equilibration, the initial slope of the clearance represents the mean ventilation per unit volume of the region. After a single-breath, where the initial distribution is flow- and not volume-weighted, the mean ventilation per unit volume is proportional to the peak height (H) divided by the area (A) under the curve.

There are pros and cons in each method. The clearance techniques give absolute values but spatial resolution is poor because large areas must be chosen to overcome statistical problems. The single or multi-breath technique gives relative values only but, particularly with $^{81}Kr^m$, a more detailed topography. The shape of the clearance curve on a logarithmic plot may give some information about fast and slow pools but the latter part of the curve can be significantly influenced by radioactivity which recirculates back to the lung or gets into the chest wall.

2.3 *Measurement of regional blood flow*

When gases are used, there are again two principal methods. First, soluble gases such as $C^{15}O_2$ can be inhaled. After a single breath, their clearance from the lung field during a subsequent breath-holding period is proportional to flow per unit water (tissue and capillary blood) volume (West and Dollery, 1960). Second, insoluble gases such as ^{133}Xe, or in our case ^{13}N or $^{81}Kr^m$, can be dissolved in dextrose or saline and injected intravenously. On their arrival in the pulmonary capillaries, 80–95% of the radioactivity (depending on their blood-gas partition coefficient) is evolved into alveolar gas where it is available for immediate counting. As for ventilation (see 2.2), a second measurement following equilibration is usually made to obtain regional perfusion per unit volume. The clearance of infused $^{81}Kr^m$ or ^{13}N during subsequent ventilation is of interest because any delay or the presence of a slow phase indicates poor ventilation of perfused tissue (*i.e.* low $\dot{V}_A/\dot{Q}$ units) within the counting field (see section 3.1).

2.4 *Vascular and extravascular volumes*

Double-indicator dilution theory (Chinard, 1975) can be applied to measurements of the transit times through lung regions for diffusible and non-diffusible tracers. Clasically, an intravascular tracer (Evans blue or Cardio green) and a water marker such as tritium (THO) are injected into the right atrium and are sampled downstream to the lung in a systemic artery. For each tracer the mean transit time is proportional to its volume of distribution between injection and sampling site divided by its rate of flow in blood. In its simplest form:

$$V_{evw} = V_w - V_b = \dot{Q}_w(\bar{t}_w - \bar{t}_b) \quad \ldots\ldots(1)$$

where V_{evw} is the extravascular water volume, V_w and V_b are the volumes of distribution of the tritium and vascular tracers, $\bar{t}_w$ and $\bar{t}_b$ are the mean transit times for the water and vascular tracers and $\dot{Q}_w$ is the water flow in blood (measured blood flow × 0.83). For regional measurements, $H_2{}^{15}O$ can be substituted for tritium and $^{113}In^m$, which binds to plasma transferrin, is a convenient plasma intravascular label. Since regional $\dot{Q}_w$ is difficult to measure in absolute terms, and relative values ($\dot{Q}_w$/unit volume) would require equilibration with ^{13}N to estimate local alveolar volume, Fazio *et al.*, (1976) suggested the use of the ratios regional extravascular water per unit blood flow ($ELW_r/\dot{Q}$) and per unit blood volume (ELW_r/Q), *i.e.*:

$$ELW_r/\dot{Q} = \bar{t}_w - \bar{t}_b \quad \ldots\ldots\ldots\ldots(2)$$

$$ELW_r/Q = (\bar{t}_w - \bar{t}_b)/\bar{t}_b \quad \ldots\ldots\ldots\ldots(3)$$

2.5 *Diffusion*

The rate of transfer of gases from the alveolus to capillary blood is usually estimated from the rate of uptake of carbon monoxide. The principles involved in the measurement of alveolar transfer rates using $C^{15}O$ have been set out by West *et al.* (1962). Following a rapid inhalation the removal of $C^{15}O$ from a lung counting field is the sum of two processes, (A) transfer from alveolar gas to capillary blood and (B) removal of labelled blood from the counting field by blood flow. The rate of diffusion (step A) is much slower than washout of the vascular bed (step B) and is rate limiting. Therefore, except in regions where blood flow is much reduced, the rate of disappearance of $C^{15}O$ from the counting field reflects diffusion and not blood flow. The rate of removal of $C^{15}O_2$, which is highly diffusible because of its conversion to $H_2{}^{15}O$ and which leaves alveolar gas with a rate constant of 2 sec^{-1}, can be used to correct the removal rate of $C^{15}O$ (rate contsant 0.07 sec^{-1}) for any effects of blood flow. The $C^{15}O_2$ correction to the $C^{15}O$ clearance rate is negligible if the $C^{15}O_2$ rate constant exceeds 0.3 sec^{-1}; even so, $C^{15}O_2$ overestimates considerably the transit time through the capillary bed in which the $C^{15}O$ is distributed, because it enters the extravascular water pool (200 ml) in addition to the peripheral blood pool (80 ml).

3. POSITRON EMITTERS

3.1 *Nitrogen-13*

Nitrogen-13 is a very insoluble gas which can be used to measure regional pulmonary blood flow, ventilation and alveolar volume in the same way as ^{133}Xe. Its insolubility means that regional ventilatory clearance can be measured accurately through at least two decades, because the amount of ^{13}N taken up into the body tissues and the chest wall is small. Most tissues will take up ten times more xenon than nitrogen and this leads to errors when the lung clearance of ^{133}Xe is measured (Matthews and

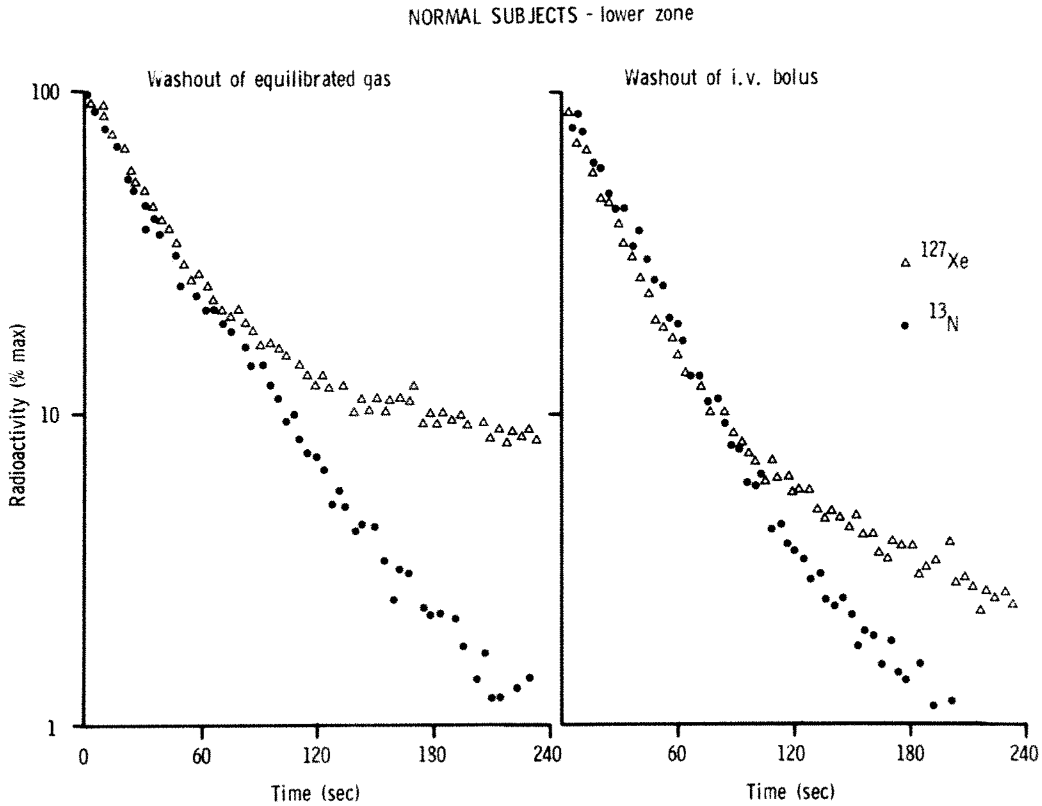

Fig. 2.

Clearance of ^{127}Xe and ^{13}N (as percent initial activity) plotted against time for the right lower zone of a normal subject after equilibration for two minutes (left) and after intravenous injection (right) with first one, then the other gas. Note also faster clearance after the *i.v.* bolus than with the equilibrated gas. (From Ronchetti *et al.*, to be published.)

Dollery, 1965). Figure 2 compares the lung clearance of ^{127}Xe, which has the same solubility as ^{133}Xe but a higher γ-emission (200 keV), with the less soluble ^{13}N. Both gases were breathed to equilibrium and also injected *i.v.* and the lower zone clearance monitored with a camera. The deviation of ^{127}Xe from ^{13}N is clearly shown. The more soluble xenon is taken up by blood in the lung and distributed to all body tissues. In an exsanguinated animal without pulmonary blood flow, the wash-in and wash-out of ^{133}Xe and ^{13}N during artificial ventilation are identical. During a continuous intravenous infusion, the retention of ^{133}Xe in the aorta, as a percent of that in the pulmonary artery, is 15% compared with 2–4% for ^{13}N (Ronchetti *et al.*, 1975a). Activity in the chest wall, which is counted more efficiently than that in the lung, or activity returning to the lung from "tissue washout", delays the latter part of the xenon clearance curve relative to nitrogen. Nevertheless, the first part of the ^{133}Xe clearance is relatively free from artefact since the alveolar concentration is much higher than that in the chest wall.

With ^{13}N considerable interest has focused upon the shape of the regional clearance itself and the differences between the washout following gaseous equilibration with ^{13}N gas and that following an intravenous injection of a ^{13}N solution. Gravity-dependent differences in ventilation per unit volume between apex and base of the lung are well known. In addition, when Rosenzweig *et al.* (1969; 1970) looked at ^{13}N clearance following equilibration from lung regions of minimal vertical height to lessen the effects of gravity, the clearances for each region, in normal subjects in the erect posture, were slightly alinear, suggesting a degree of intra-regional inhomogeneity, independent of gravity. Rosenzweig *et al.*, were unable to decide whether this represented series or parallel inequalities in local ventilation or even intrinsic differences between lung lobes which overlapped in the counting field. Ewan *et al.* (1978), also in normal subjects and in the erect posture, found that the clearance of an intravenous bolus of ^{13}N, which labels units in proportion to their blood flow, was slightly but significantly faster than the clearance of ^{13}N after closed-circuit equilibration when units are labelled in proportion to their volume. This is clearly shown in Fig. 2. From this observation, they inferred that within lung regions (A) there was non-uniform ventilation (as already shown by Suda *et al.* (1970) and (B) that the better ventilated units were also better perfused.

This difference of function within regions is much more obvious in patients with chronic bronchitis and emphysema (Eiser *et al.*, 1977) where the clearance of the injected ^{13}N was up to 50% faster than that for equilibrated ^{13}N. This difference was reduced if the patients breathed 30% oxygen for 15 minutes. The authors concluded that oxygen breathing had reversed the hypoxic vasoconstriction of the pulmonary arterial vessels supplying the more poorly ventilated units within the counting region, enabling them to receive a larger share of the local blood flow and thus of the radioisotopic marker, hence the slower clearance. The washout after ^{13}N equilibration, which labels units in proportion to their volume not their blood flow, was unaffected by oxygen breathing. This suggests that oxygen did not affect the distribution of ventilation. Clearance curves in patients with airway disease are also considerably less linear on a semi-log plot (Fig. 3), indicating maldistribution within regions as well as that seen between regions with $^{81}Kr^{m}$ (see section 4.3).

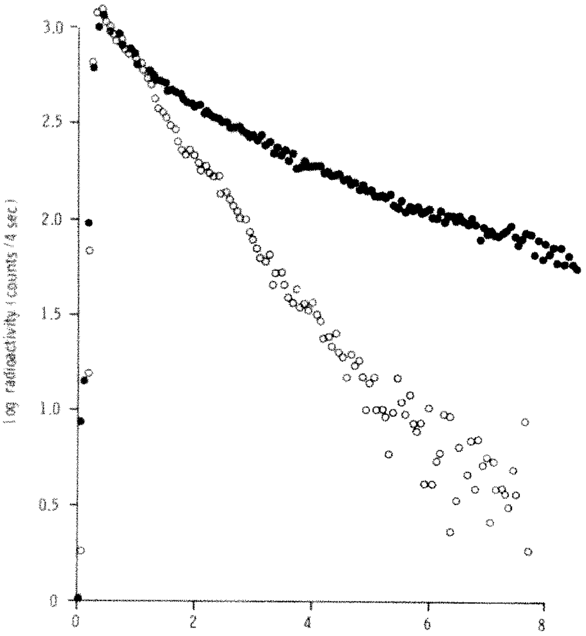

Fig. 3.

Comparison of regional (mid-zone) clearance of ^{13}N, given by *i.v.* injection, in a normal subject (○) and in a patient with chronic bronchitis (●). Logarithm of counts plotted against time. Note the slow and multiexponential clearance in the patient compared with the rapid almost linear decay in a normal subject. Clearance after *i.v.* injection reflects the ventilation of perfused units. The slow phase in the patient suggests the presence of units with low $\dot{V}_A/\dot{Q}$ and a low oxygen tension (see text).

^{13}N has also found a place in the study of infants with cardiopulmonary disorders (Ronchetti *et al.*, 1975b; Godfrey and McKenzie, 1977). The radionuclide, dissolved in saline, is injected into a peripheral vein, or inhaled as a bolus of gas through a nasal catheter with its tip in the pharynx. The child, suitably sedated, lies on the gamma camera and the washout of inhaled and injected ^{13}N is recorded for two regions in each lung. The only requirement is that the baby lies still. Recently, McKenzie *et al.* (1977) reported that the clearance of ^{13}N by ventilation after its administration intravenously was delayed in children with severe pulmonary hypertension and (usually) a right to left shunt. Since the clearance of inhaled ^{13}N was normal, the authors suggested that there was a population of perfused but virtually unventilated alveoli in these circumstances. Their results must be interpreted with caution since, in the presence of a right to left shunt, ^{13}N getting into the chest wall or recirculating back to the lung could give a similar picture.

Using a positron camera, some interesting images of the distribution of an inhaled bolus of ^{13}N (showing the influence of airway closure) have been obtained (Hales *et al.*, 1976).

3.2 *Oxygen-15 labelled H_2O*

$H_2{}^{15}O$ can be used to measure extravascular lung water (ELW); see section 2.4. In seven supine normal subjects, Fazio *et al.* (1976) injected $H_2{}^{15}O$ and $^{113}In^{m}$ solutions separately into the subclavian vein and recorded time activity curves over two lung regions with pairs of counters. Regional extravascular lung water per unit blood volume (section 2.4) was 0.38 and per unit blood flow was 2.08 sec. There was no difference between apex and base. Overall ELW was estimated at 172 ml$\pm$54 (mean $\pm$1 SD) which gives a blood volume from injection in the superior vena cava to the largest veins in the counting field of 450 ml. In patients with left heart failure, the values (averaged for both regions) were approximately double, 0.7 and 4.7 sec respectively, with more ELW in the basal (caudal) zone. The ratio ELW_r/blood volume probably reflects changes in local extravascular water content more closely than ELW_r/blood flow. The latter index is sensitive to any redistribution of local perfusion and to overall cardiac output which was 33% less in the patients. Nevertheless, in the patients both indices varied in proportion to the value of left atrial pressure and to the presence of interstitial oedema. Binswanger *et al.* (1978) repeated these measurements in similar groups of subjects, substituting ^{123}I-antipyrine for $H_2{}^{15}O$. Their values for ELW_r/blood volume were almost indentical to those of the Hammersmith group, but the values for ELW_r/blood flow were 1.7 to 2.7 times greater, probably due to a different method of calculating mean transit time (area/height rather than ratio of moments used by the Hammersmith group).

Studies in isolated lungs suggest that injected $H_2{}^{15}O$ may underestimate extravascular water content, either total (Dollery and Matthews, 1971) or regional (Jones *et al.*, 1976), presumably because of an uneven distribution of blood flow. Local blood flow may be reduced in regions where there is the severest oedema. Thus, there is a tendency for $H_2{}^{15}O$ to be diverted through the least oedematous parts of any lung region. On the other hand, the most recent measurements from our laboratory in isolated lobes have shown that changes in regional $H_2{}^{15}O$ mean transit times correlate closely with changes in weight as the lobes become oedematous (Heather *et al.*, 1978).

3.3 *Oxygen-15 and carbon-11 labelled CO_2*

The factors determining the clearance rate of these compounds were worked out by West, Dollery and their colleagues in the early 1960's. A 30–50 ml bolus of $C^{15}O_2$ gas is generally given at the beginning of a rapid inspiration, and its arrival in different regions of the lung and subsequent clearance during a ten second breath-hold is monitored by two or more pairs of counters placed over the chest. The transfer of $C^{15}O_2$ from alveolar gas into lung tissue and blood occurs so rapidly (the rate constant is about 2.2 sec^{-1}) that it is difficult to measure (West and Dollery, 1962). The rapid transfer depends on two factors; first, the rapid diffusion of CO_2 and second the ^{15}O label. In the blood and tissues of the lung the oxygen label is mainly present in the form of bicarbonate which, under the influence of carbonic anhydrase, rapidly exchanges with the hydroxyl ion of water. Thus, ^{15}O enters the water pool of the lung almost instantaneously following a rapid and deep inhalation and virtually no activity remains behind in alveolar gas. Carbon-11 labelled CO_2 diffuses as rapidly but remains as bicarbonate where it is in equilibrium with lung CO_2; its removal from alveolar gas is ten times slower than $C^{15}O_2$.

The clearance of $C^{15}O_2$ during apnoea represents blood flow per unit tissue volume; therefore, in situations where tissue volume is abnormal, as in pulmonary oedema, the clearance of $C^{15}O_2$ will be slowed (Dollery *et al.*, 1962; Schmidt-Nowara *et al.*, 1973). There are several problems in such a simple approach, the major one being the requirement of a independent measurement of regional blood flow. In most cases of pulmonary oedema, secondary to left heart failure, the cardiac output is low and this will slow the $C^{15}O_2$ clearance. In fact, a local "hold-up" of inhaled $C^{15}O_2$ can be seen in clinical pulmonary embolism (Nichols *et al.*, 1978). Secondly, if the oedematous areas cease to ventilate and become inaccessible to the inhaled tracer, the $C^{15}O_2$ clearance may be little changed. Nevertheless, A. J. Swinburne's recent measurements from our laboratory show this is not to be the case. As isolated lobes became oedematous, the slowing of the initial slope of the $C^{15}O_2$ clearance, with a constant pulmonary blood flow, was proportional to the increase in weight (Fig. 4).

We pointed out recently (Pande *et al.*, 1976; Hughes, 1977) that the regional clearance of $C^{15}O_2$ in normal subjects during breath-holding has fast and slow components, with rate constants of about

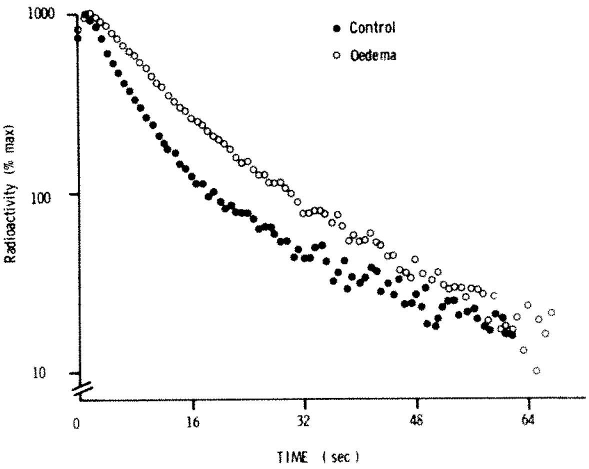

Fig. 4.

Clearance of a single inhalation of $C^{15}O_2$ during breath-holding from an isolated dog lobe in the absence of recirculation. Radioactivity in counts per sec as % of initial activity, plotted on a log scale against time. Measurements were made in the control situation and in oedema (after 57% weight gain). Flow remained constant. The increase in clearance time was 56%, i.e. equal to that predicted from the increase in total lung water volume. (From A. J. Swinburne *et al.*, to be published.)

0.6 sec^{-1} and 0.1 sec^{-1} respectively. We speculated that the fast component might represent direct access of $C^{15}O_2$ into the vascular compartment with equilibrium with the tissue pools taking longer. Similar findings and conclusions were reached by Schmidt-Nowara *et al.* (1973) on the basis of experiments in isolated perfused lungs. Further work in isolated lobes in which there is no recirculation and in subjects who inhaled $C^{15}O_2$ into one lung via an intrabronchial catheter (MacArthur *et al.*, to be published), has now shown that the slow component is an artefact caused by early reappearance of ^{15}O (as $H_2{}^{15}O$) via the bronchial or intercostal (chest wall) circulations. Therefore, analysis of $C^{15}O_2$ clearance curves, in the intact animal, should be limited to the initial slope which, in isolated lobes, is a good monitor of the increase in lung weight in oedema (see previous paragraph).

3.4 *Oxygen-15 labelled CO*

The diffusion of carbon monoxide from alveolar gas to pulmonary capillary blood depends on the tissue diffusivity of CO, the surface area and thickness of the alveolar capillary membranes, the rate of reaction of CO with haemoglobin and the number of haemoglobin combining sites, *i.e.* the local blood pool. In normal lungs, differences in uptake of $C^{15}O$ between regions are related almost entirely to differences in the last factor, the local capillary blood volume. For example, following a single inhalation, there is a gradient of increasing uptake of $C^{15}O$ with distance down the vertical lung with an upper/lower zone ratio of 0.48 (Ewan *et al.*, 1976). This is consistent with the vertical gradient of blood volume which has been shown in isolated perfused dog lungs, using ^{11}CO-labelled red cells (Jones *et al.*, 1975). J. Pande, in our laboratory, has shown that

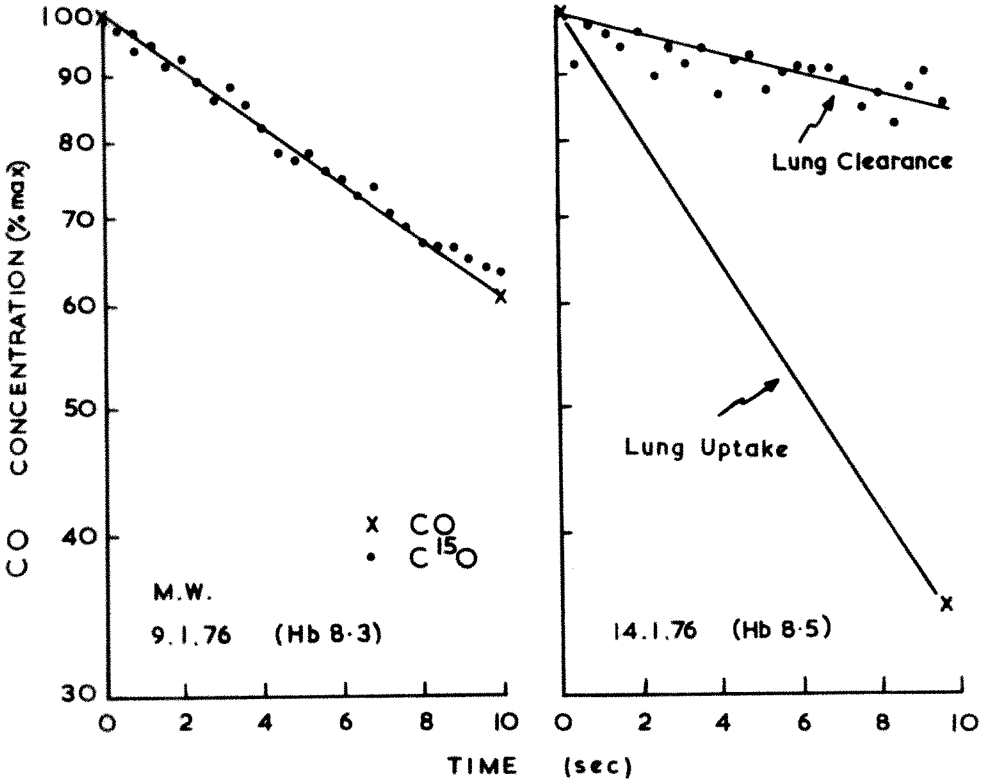

Fig. 5.

Lower zone clearance of inhaled $C^{15}O$ on a long scale against time during breath-holding, in the presence (right) and absence (left) of a stagnant pool of blood. Measurements made on two occasions (see dates) in a patient with Goodpasture's syndrome. Measurements of the removal of CO from the gas phase (lung uptake) using non-radioactive carbon monoxide are also shown. Note that bleeding leads to an increased uptake of carbon monoxide from alveolar gas but slows the clearance of CO from the lung field. (From Ewan *et al.* (1976), with permission.)

$C^{15}O$ uptake increases during exercise in normal subjects, the relative increase being greatest in the upper zones (see Table II). Similar results have been shown for blood flow on exercise by Harf *et al.* (1978) using $^{81}Kr^{m}$. This phenomenon of apical recruitment of blood flow and capillary blood volume strikingly demonstrates the gas-exchanging reserve of the lung.

An interesting clinical application of the use of $C^{15}O$ has been the detection of stagnant pools of blood in Goodpasture's syndrome (Ewan *et al.*, 1976), a condition characterized by nephritis and lung haemorrhage. As Fig. 5 shows, the lower zone clearance of $C^{15}O$ was considerably slowed at a time when the uptake from alveolar gas (measured by sampling inspired and expired air) was greatly elevated. We believe this is caused by a stagnant pool of blood which can take up CO. Although a similar picture might be seen in a zone with low or absent blood flow, *e.g.* pulmonary embolism or infarction, as has been shown in experimental pulmonary embolism by Taplin *et al.* (1976), the clearance of $C^{15}O_2$ was not noticeably different between the two measurements. From the rate constants (λ) the ratio of extravascular to intravascular blood is given by $\frac{\lambda C^{15}O(a)}{\lambda C^{15}O(b)} - 1$, where (a) and (b) refer to the non-bleeding and bleeding states respectively. In this example, the ratio is 5.9; assuming 40 ml of blood in the capillary vessels of the lower zones, this represents 236 ml of extravascular blood.

TABLE II

LUNG UPTAKE OF $C^{15}O$ (% SEC^{-1}) DURING BREATH HOLDING AT REST AND DURING EXERCISE (50 WATT). MEAN RESULTS IN FOUR NORMAL SUBJECTS, SEATED ERECT. (FROM PANDE ET AL., TO BE PUBLISHED.)

Region	Rest	Exercise	Exercise/Rest
Upper	2.4	5.55	2.3
Mid	4.8	7.13	1.5
Lower	6.6	8.2	1.24

4. KRYPTON-81M

4.1 *Theory*

This 13-second half-life radionuclide was first used as a bolus to measure the distribution of ventilation and blood flow (Jones *et al.*, 1970) but it did not become a practical proposition as a clinical tool until a continuous inhalation technique was used (Fazio and Jones, 1975). The principle is set out in Fig. 6 (Jones *et al.*, 1975). When an insoluble

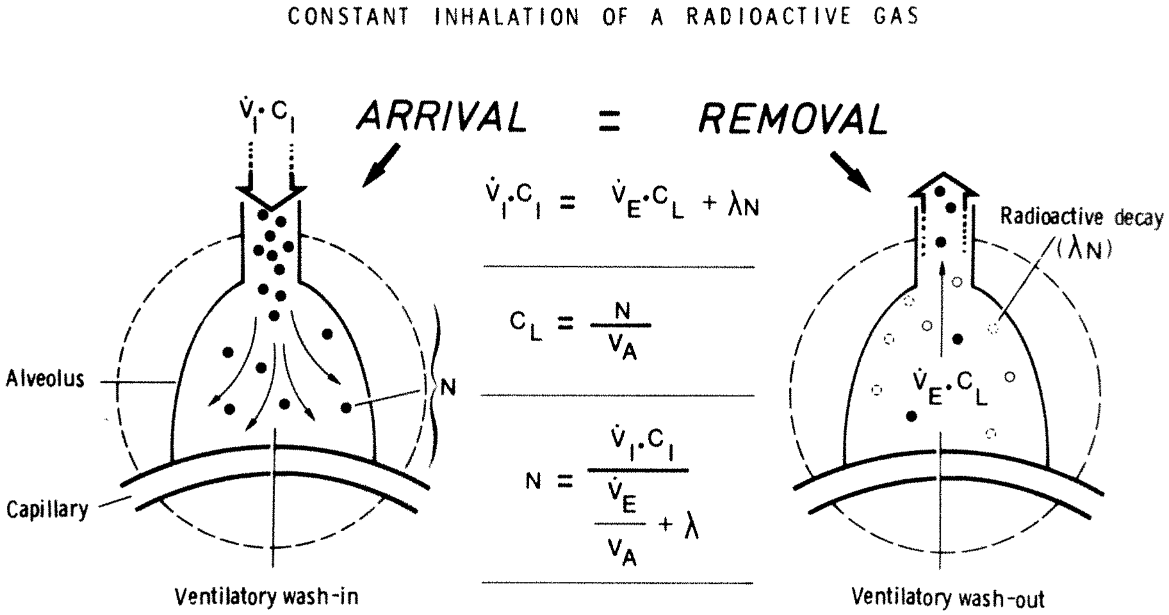
CONSTANT INHALATION OF A RADIOACTIVE GAS
$\dot{V}_I \cdot C_I$
ARRIVAL = REMOVAL
$\dot{V}_I . C_I = \dot{V}_E . C_L + \lambda N$
$C_L = \frac{N}{V_A}$
$N = \frac{\dot{V}_I . C_I}{\frac{\dot{V}_E}{V_A} + \lambda}$
Alveolus
Capillary
N
Radioactive decay (λN)
$\dot{V}_E . C_L$
Ventilatory wash-in
Ventilatory wash-out

FIG. 6.

Determinants of regional count rate with continuous inhalation of a short half-life insoluble radioactive gas, such as $^{81}Kr^{m}$. $\dot{V}_I$ and $\dot{V}_E$ represent inspired and expired ventilation, C_I and C_L the concentration of radioactivity in inspired gas or in the alveolar compartment of the lung, N the number of radioactive molecules and hence the regional counts per second, λ the rate constant of radioactive decay (3.2 min^{-1} for $^{81}Kr^{m}$), and V_A the local alveolar volume. $\dot{V}_E/V_A$ is alveolar ventilation per unit volume; the interrupted circle represents the counting field.

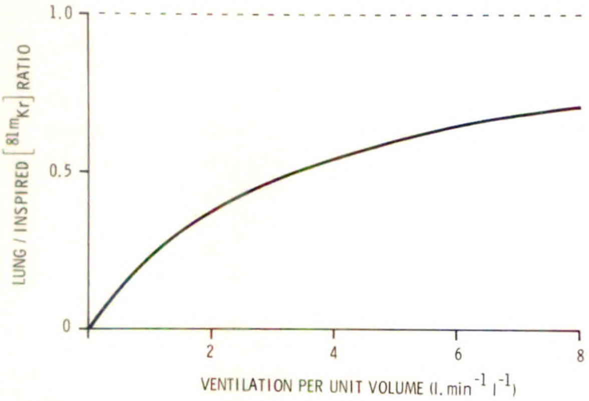

FIG. 7.

Relationship between steady-state count rate from ^{81}Kr^{m}, as a percentage of that inspired, and alveolar ventilation in a unit of constant volume. In the absence of radioactive decay, equilibrium between inspired and alveolar concentrations occurs with insoluble gases as shown by the interrupted line. For ^{81}Kr^{m}, curvilinearity is related to $\dot{V}_I C_I/(\dot{V}_E/V_A+\lambda)$ as in Fig. 6.

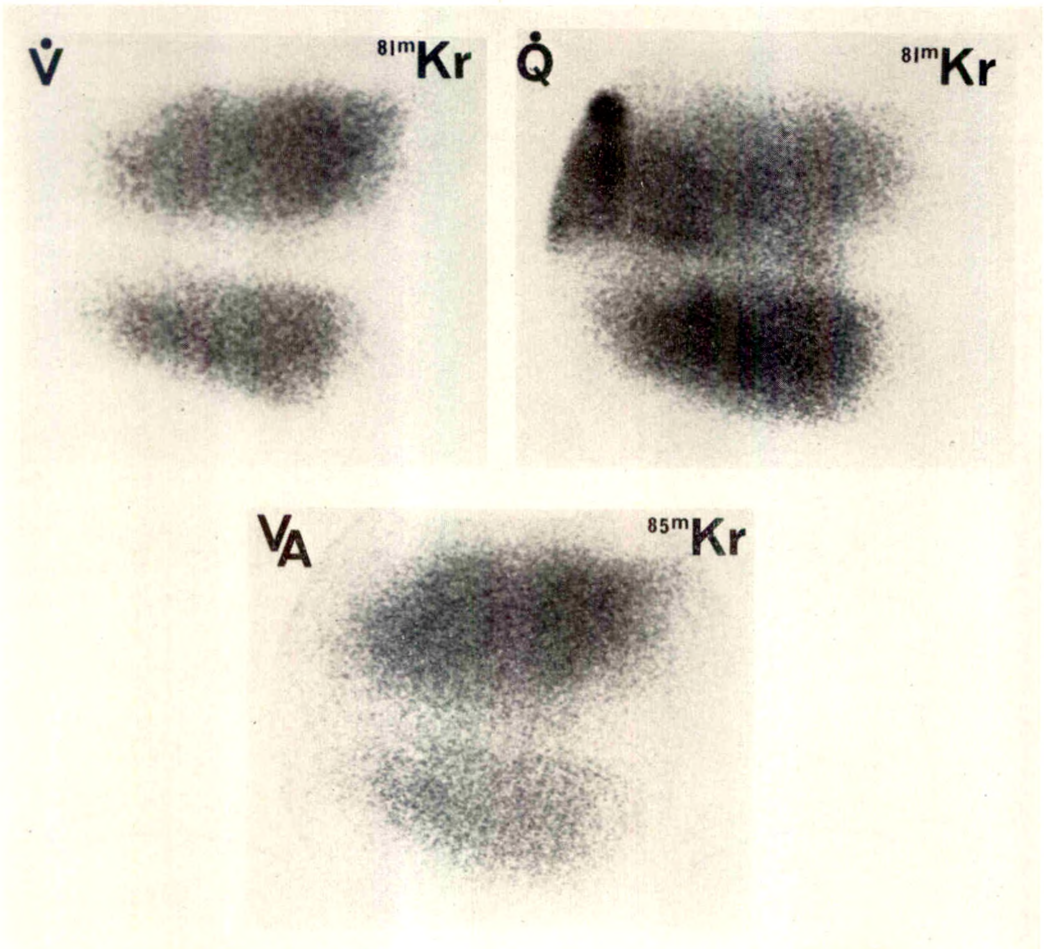

FIG. 8.

Radioactivity distributions, in steady state, during ^{81}Kr^{m} inhalation ($\dot{V}$), intravenous infusion ($\dot{Q}$) and after rebreathing the long half-life ^{85}Kr^{m} (V_A), in a normal subject in the left lateral decubitus posture. The $\dot{V}$ image (^{81}Kr^{m}) looks similar for the top and bottom lung, but this is partly due to the larger volume of the upper lung, as seen in the ^{85}Kr^{m} image. The true ventilatory turnover of the lower lung is more than double that of the upper—2.25 compared with 0.95 min^{-1}. (From Amis *et al.* (1978) with permission.)

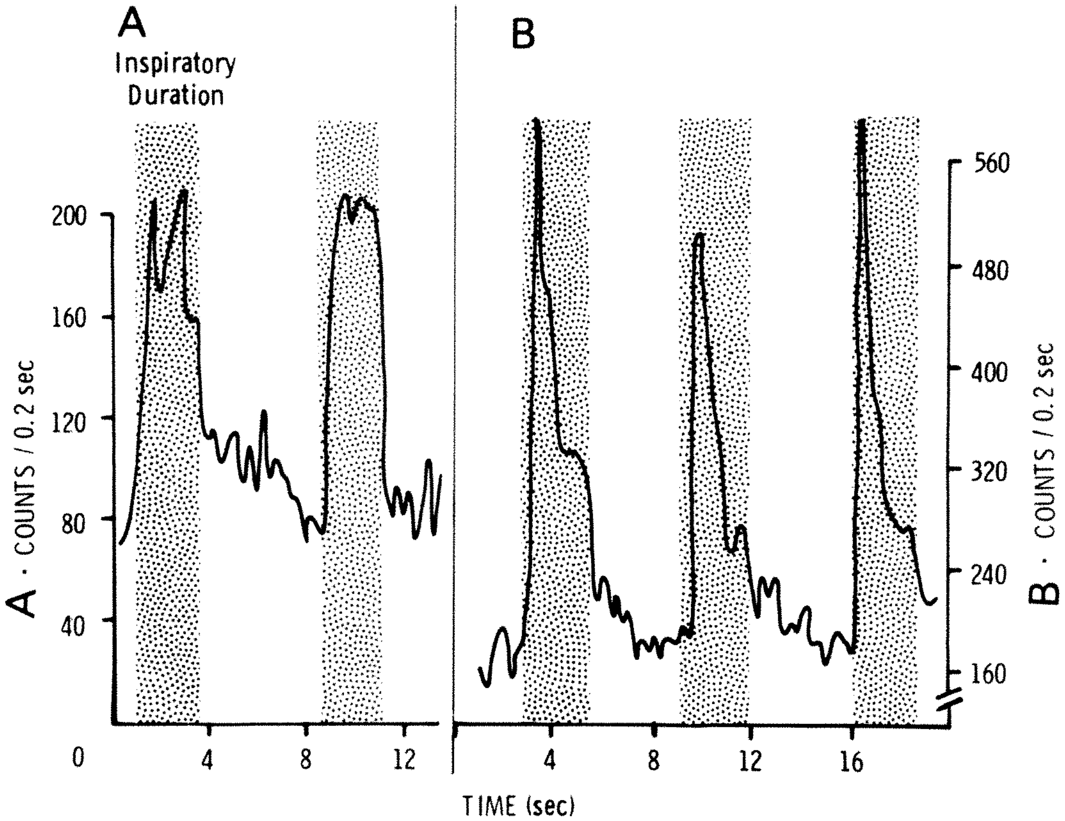

Fig. 9.

Time-activity curve over the trachea during inspiration when $^{81}Kr^{m}$ is delivered at the mouth during normal breathing from a reservoir with overflow (A) compared with administration from a face mask (B).

marker gas is inhaled continuously in open circuit, a steady state is reached when the arrival of gas molecules in any region of the lung is equal to the removal. For example, when breathing air, the arrival and removal of ordinary nitrogen molecules from our lungs is virtually identical and the concentrations of nitrogen in inspired and expired air are almost equal. Thus, the number of nitrogen molecules in our lungs reflects their volume. This principle has long been used to measure the volume of lungs; in practice, an insoluble marker such as helium (or ^{13}N or ^{133}Xe for regional volumes) is rebreathed in closed circuit, and the dilution determined. The intriguing property of gases with half-lives of less than 20 seconds is that the concentration in the lung will never reach that inspired unless expired ventilation is much faster than radioactive decay. As illustrated in Fig. 6, the removal process is the sum of ventilatory washout ($\dot{V}_E.C_L$) and radioactive decay. For insoluble gases, any additional removal by pulmonary blood flow is negligible. Similarly, radioactive decay can be neglected for most radionuclides. But for $^{81}Kr^{m}$, radioactive decay at a rate of 3.2 min^{-1} is more important than the lung washout of this isotope (1.5–2.0 min^{-1}). Up to ventilatory turnovers of 2 min^{-1}, the local $^{81}Kr^{m}$ count rate increases fairly linearly with ventilation in a unit with constant volume (Fig. 7). In practice, the count rate is volume as well as ventilation sensitive, and the detector records the influx of radioactivity—the inspired volume per unit time—and not the true turnover, *i.e.* the ventilation per unit volume. The influence of volume on the ventilation image is shown in Fig. 8 (Amis *et al.*, 1978).

4.2 *Technique*

The administration of $^{81}Kr^{m}$ is simple. The radioactive gas is continuously eluted from the ^{81}Rb generator with a flow of about 1 l/min from a compressed air cylinder. The dry gas must be adequately humidified before it passes across the ion-exchange resin column containing the ^{81}Rb. The radioactive gas is added at a constant flow rate to the mouthpiece or face mask (transparent disposable type) from which the subject is quietly breathing. 250×10^3 counts are generally accumulated over a period of 30–90 seconds, depending on the activity of the generator. The window of the Anger gamma camera is set at 190 keV ($\pm$15–20%); in routine studies of distribution of ventilation and perfusion, $^{99}Tc^m$-microspheres are injected for the lung perfusion image because an infusion of $^{81}Kr^m$ for the recording of blood flow (see section 4.5) would require a second ^{81}Rb generator. After the ventilation scan and without changing position, the $^{81}Kr^m$ supply is discontinued, the energy window is reset for $^{99}Tc^m$ at 140 keV, and the lung perfusion image recorded. This procedure is repeated in the anterior, right and left lateral positions. The $^{99}Tc^m$ breakthrough into the 190 keV window is 10–15%.

When $^{81}Kr^m$ gas is added continuously to face masks or mouthpieces, the concentration of radioactivity during inspiration varies considerably. Because of the small reservoir of these devices, $^{81}Kr^m$ activity builds up towards the end of expiration, giving a sharp burst of activity at the beginning of the next inspiration (see Fig. 9B). As inspiratory flow builds up, so the level of activity in inspired gas falls. We have designed an input reservoir in which the subject, on a mouthpiece, inhales from a bag which is continuously flushed with $^{81}Kr^m$ at 1 l/min and air at 12 l/min (*i.e.* at more than the subject's ventilation). The excess inflow to the reservoir overflows to waste. This device produces a constant inspired concentration but cuts the count rate in half (Fig 9A). Without the use of a reservoir, the $^{81}Kr^m$ ventilation image is weighted towards the initial part of inspiration. Normal subjects show a small degree of sequential ventilation but the difference between the regional distribution of inspired gas early and late in inspiration is small (Grant *et al.*, 1974). The effects might be much greater in patients with airflow obstruction and the "bolus" method of administration (Fig. 9B) might mask or (more probably) exaggerate

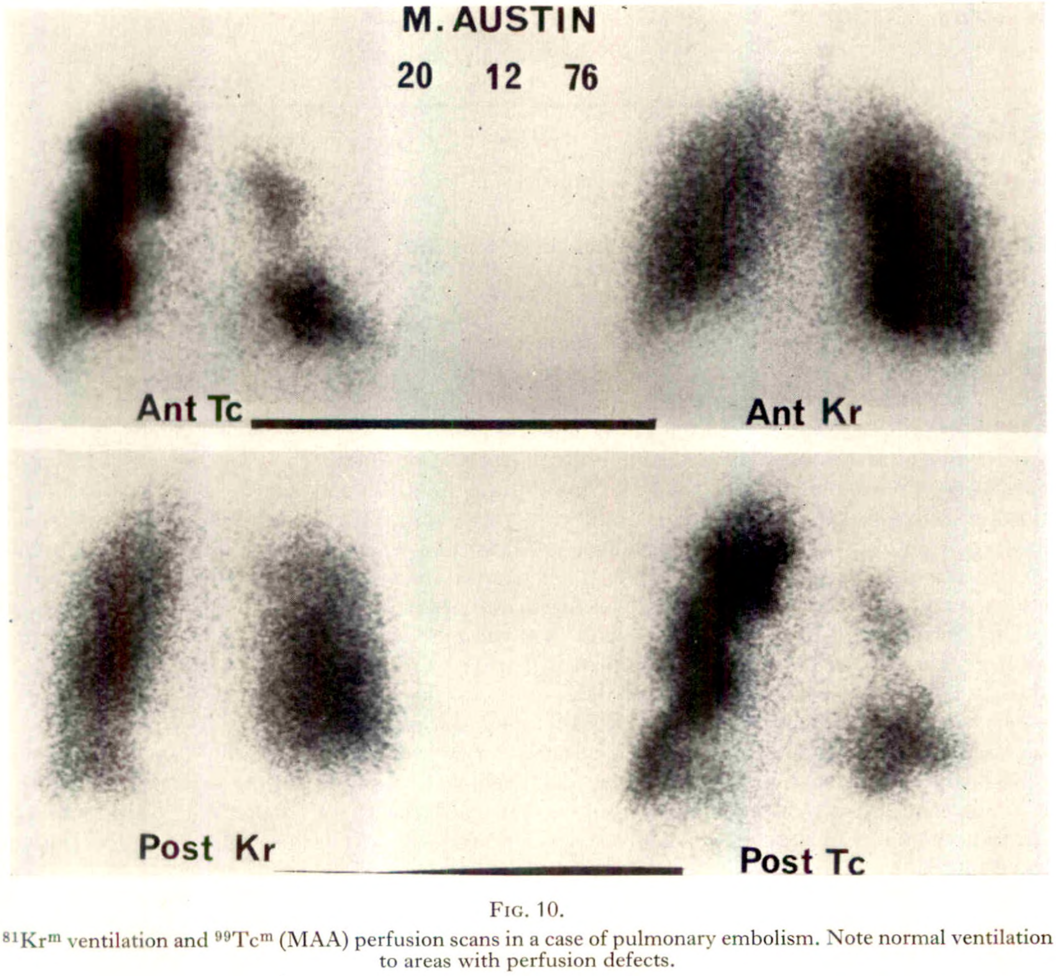

Fig. 10.

$^{81}Kr^m$ ventilation and $^{99}Tc^m$ (MAA) perfusion scans in a case of pulmonary embolism. Note normal ventilation to areas with perfusion defects.

regional inequalities of ventilation. The matter needs to be investigated further.

4.3 *Clinical use*

For clinical diagnosis, the qualitative information provided by the ^{81}Kr^{m} ventilatory scan has proved useful. In terms of spatial resolution, depth response, radiation dosage and ease of administration, ^{81}Kr^{m} holds advantages over ^{133}Xe. The distribution of ventilation can be recorded in multiple views in a single subject in a few minutes. The ^{81}Kr^{m} ventilation scan is a companion to the more familiar ^{99}Tc^{m} lung perfusion scan. The images for each on photographic film look similar and a quick clinical assessment can be made. For example, there are many causes of perfusion defects on the ^{99}Tc^{m} scan, but if the ^{81}Kr^{m} ventilation scan shows a uniform pattern, vascular obstruction due to pulmonary embolism is extremely likely (Fig. 10). The segmental nature of the perfusion defect is sometimes seen best in lateral or oblique views. It is often difficult to diagnose pulmonary embolism if there is a background of respiratory disease. In chronic bronchitis and emphysema defects of perfusion and ventilation tend to occur in the same regions of lung. If they develop pulmonary embolism, two types of blood flow defect may be seen—those with and those without an accompanying ventilatory abnormality. The presence of so-called "unmatched" defects (absent perfusion with ventilation maintained) suggests pulmonary embolism. Pulmonary infarction can usually be distinguished from pneumonia because of the persistence of blood flow in the latter, although the ^{81}Kr^{m} scan will be abnormal in both circumstances. Pulmonary embolic disease, in its acute phase, may be accompanied by ventilatory defects secondary to reflex bronchoconstriction. Nevertheless, if the chest radiograph is normal, the ventilatory defect is usually transient; since embolic disease is multifocal, careful examination of other parts of the lung in other views will often show the classical unmatched defects of embolism (J. P. Lavender, personal communication).

Apart from pulmonary embolism, ventilation scanning of the lung may be clinically helpful in the pre-operative assessment of bronchial carcinoma (Lipscomb and Pride, 1977). In cases of pneumonectomy, the ventilatory scan gives a useful prediction of post-operative function. Neither the ventilation (^{81}Kr^{m}) nor perfusion (^{99}Tc^{m}) scans made pre-operatively are accurate predictors of mediastinal involvement, unless the defects are unexpectedly large.

The airflow obstruction in patients with chronic bronchitis and asthma is associated with large segmental defects in the ^{81}Kr^{m} ventilation scan in the presence of a normal chest radiograph (Fazio *et al.*, 1978). This is not particularly surprising since the radiograph detects major anatomical lesions rather than functional changes and airway narrowing or mucus plugging would not be seen on the plain film. Nevertheless, the topography of the ventilatory abnormalities and their resolution with treatment is of interest (Fazio *et al.*, 1978; Fazio and Jones, 1975).

The ventilation scans show large differences in function between adjacent segments. This does not mean that the site of obstruction is necessarily in the segmental bronchus, but it does imply that resistance to collateral ventilation, which prevents the segment from collapsing, is high.

The information contained in a single ^{81}Kr^{m} inhalation scan is a fairly crude representation of regional ventilation in relative terms. In chronic bronchitis, for example, a patchy ventilation image is observed as if normal areas existed alongside abnormal ones. In fact, if regional ventilation is expressed in absolute units (in min^{-1}) by measuring a ^{13}N washout, all areas are grossly abnormal, the difference in the ^{81}Kr^{m} lung scan being merely one of degree. In addition, no allowance is made for geometric factors (*i.e.* ventilation per unit volume) or the alinear relationship between radioactivity and ventilation shown in Fig. 7. There is also considerable dispersion of function within even small regions (Suda *et al.*, 1970; see also Fig. 3) which is masked by the steady state technique. Nevertheless, the count rate is high and the counting statistics very good, and the purely qualitative value of ^{81}Kr^{m} ventilation scanning can be considerably enhanced if minute to minute changes are recorded with serial images. In this way the response to drugs, to an antigen challenge or to physiotherapy can be assessed in relation to the initial control image. Figure 11 shows the effect of coughing; other studies have monitored the changes during the induction of bronchoconstriction, simulating an asthmatic attack (Hughes *et al.*, 1978).

4.4 *Quantitative measurement of ventilation*

There are several ways of obtaining quantitative information with ^{81}Kr^{m}. As mentioned above, serial images can be analysed. In a study of the distribution of infused ^{81}Kr^{m} (see section 4.5) at the start of exercise, Harf *et al.* (1978) took an area on the display matrix for the apex of the left lung which contained 5% of the counts in that lung at rest. Keeping this area of interest and the total area constant, the percentage of radioactivity (or blood flow) to the

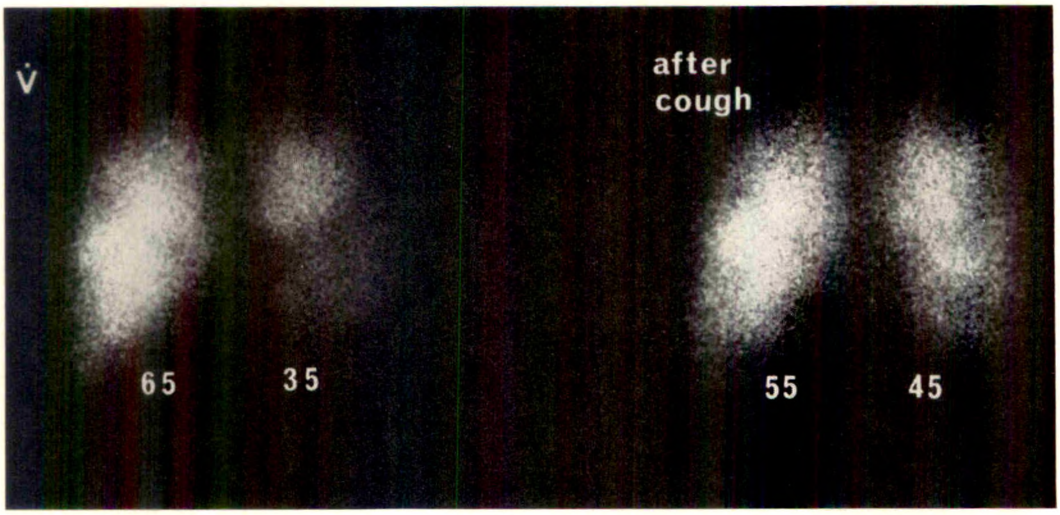

FIG. 11.

^{81}Kr^{m} inhalation scans before and after coughing in an asthmatic subject. The percentage of counts to each lung is given. The posterior view shows that the right lung, especially the lower zone, is poorly ventilated initially.

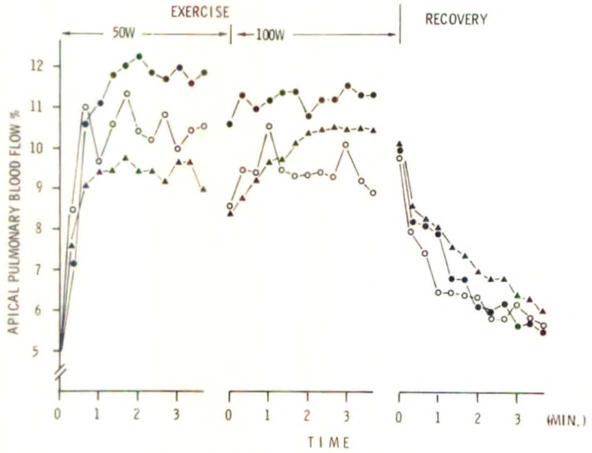

FIG. 12.

Continuous *i.v.* infusion of ^{81}Kr^{m} in three normal subjects at rest, during two levels of exercise (50 and 100 watt) on a cycle ergometer and on recovery. Radioactivity (representing pulmonary blood flow) at apex of left lung, as a percent of activity in the whole lung, plotted against time. An area of interest at the apex which contained 5% of the lung counts at rest was chosen for analysis. Note rapid increase and decrease in relative flow to top of the lung at the beginning and end of exercise period. (From Harf *et al.* (1978) with permission.)

lung apex, could be followed during and after stopping exercise (Fig. 12). Changes in the distribution of ventilation could be analysed in a similar way.

Secondly, the inhalation or infusion of ^{81}Kr^{m} can be stopped once a steady state has been reached and the washout recorded. The clearance in min^{-1}, calculated from the initial slope of radioactive decay, measures the whole removal process *i.e.* $(\dot{V}_E/V_A+\lambda)$, from which 3.2 min^{-1} (λ) must be subtracted. Because of the short half-life of ^{81}Kr^{m}, the half time of the clearance must be 13 seconds or less, and counts have to be recorded at one second intervals. In regions where ventilatory turnover is low (less than 0.7 min^{-1} compared with 1.0–2.0 min^{-1} normally), the clearance is so dominated by λ that the $\dot{V}_E/V_A$ contribution can no longer be identified. For statistical reasons, reasonably large areas must be chosen; consequently spatial resolution with this method will be poor. Nevertheless, ^{81}Kr^{m} washout may be used to give quantitative information in large regions in relatively normal lungs or where $\dot{V}_E/V_A$ is high as in children (see section 4.6). Again, the measurements can be repeated at short intervals to study the effects of different breathing patterns, changes of posture or exercise.

The best method of quantitation involves repeating the inhalation manoeuvre with a second radioactive gas which has a different λ (*i.e.* a longer half-life) with a similar γ-ray energy to ^{81}Kr^{m}. Krypton-85m (half time 4.4 hours: 150 keV) has been used. If a gas with a long half-life is added continuously to the inspirate, and if the volume of the lung remains constant, its alveolar concentration relative to that inspired will approach that of the interrupted line in Fig. 7, the local count rate being proportional to $V_A.C_I$ where V_A is the local volume of lung seen by the detector and C_I is the inspired concentration of ^{85}Kr^{m}. Assuming that the

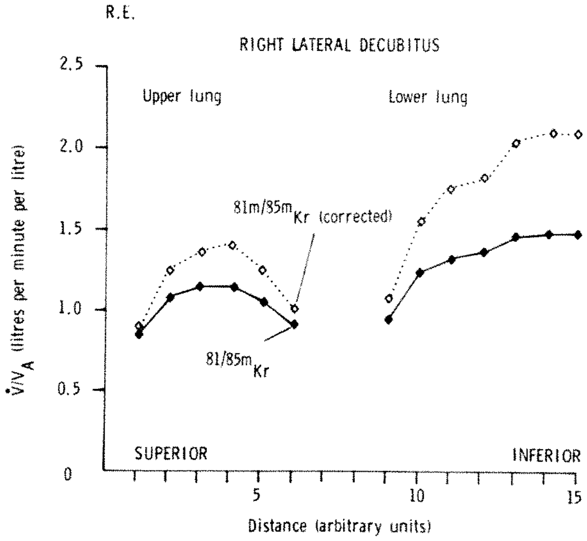

FIG. 13.

Distribution of ventilation per unit volume in a normal subject in right lateral decubitus posture, measured by ^{81}Kr^{m} inhalation followed by equilibration with ^{85}Kr^{m}. Distribution obtained by straight division of ^{81}Kr^{m} counts by ^{85}Kr^{m} counts is compared with the distribution calculated from a modification of equation 4.

geometric factors for 190 keV (^{81}Kr^{m}) and 150 keV are similar and that λ for ^{85}Kr^{m} is negligible, the equation in Fig. 8 can be solved simultaneously for ^{81}Kr^{m} and ^{85}Kr^{m} (Jones *et al.*, 1978) to give

$$\dot{V}_{E}/V_{A_R} = \lambda x/(1-x) \quad \ldots\ldots\ldots (4)$$

where $\dot{V}_{E}/V_{A_R}$ is regional ventilation per unit volume (min^{-1}), λ is the ^{81}Kr^{m} decay constant (3.2 min^{-1}) and x is the ratio of count rates (N) for lung regions (R) and inspired gas (I) for ^{81}Kr^{m} (81) and ^{85}Kr^{m} (85) *i.e.* $[(N_{R(81)}/N_{R(85)}]\cdot[N_{I(85)}/N_{I(81)}]$. Rather than measuring the inspired concentrations, Amis *et al.* (1978) have shown that the same information can be obtained if the whole lung clearance of ^{85}Kr^{m}, after the equilibration phase, is monitored (in min^{-1}) and if the regional counts for each isotope are expressed as a percentage of the counts for the whole lung. A simpler method which just divides the ^{81}Kr^{m} image (ventilation) by that for ^{85}Kr^{m} (volume) to obtain ventilation per unit volume, has two disadvantages. First, the results will be in arbitrary units rather than min^{-1}; secondly, the alinearity shown in Fig. 7 will be neglected. Figure 13 shows that regional differences of ventilation per unit volume will be underestimated if equation 4 is replaced by a straight division of the images (Amis *et al.*, 1978).

Administration of the longer-life radioisotope, ^{85}Kr^{m}, is cumbersome, particularly if patients are involved. At the present time, we collect steady state images for ^{81}Kr^{m} inhalation and infusion and then switch the subject into a closed circuit containing a spirometer, non-rebreathing valve, CO_2 absorber and about 1 mCi/litre of ^{85}Kr^{m}. A more elegant approach would be to add both isotopes simultaneously to the gas inspired, and separate the ^{81}Kr^{m} and ^{85}Kr^{m} peaks electronically.

4.5 *Distribution of pulmonary blood flow*

To measure regional perfusion, ^{81}Rb generators are perfused with 5% dextrose and ^{81}Kr^{m} eluted in solution for intravenous infusion through an indwelling ("butterfly") needle in a forearm vein. The infusion rate varies from 2 to 20 ml min^{-1} (average 10 ml min^{-1}). The theory associated with the steady state inhalation of ^{81}Kr^{m} (Fig. 6) applies, except that the arrival of the isotope is proportional to local blood flow ($\dot{Q}$) not ventilation ($\dot{V}_{I}$). The removal process is similar to that for inhaled ^{81}Kr^{m}, assuming the lung region has no maldistribution of ventilation and perfusion within it. To the extent that there is a dispersion of ventilation-perfusion ratios within a region, the regional $\dot{V}_{E}/V_{A}$ for infused ^{81}Kr^{m} will be slower than that for inhaled krypton.

In lungs which are uniformly ventilated, as judged by an ^{81}Kr^{m} ventilation scan, the distribution of continuously infused ^{81}Kr^{m} is similar to that of injected radio-labelled (^{99}Tc^{m}) human serum albumin macroaggregates. Ciofetta *et al.* (1978a) have found that pulmonary vascular defects show up equally well on the krypton and technetium lung scans. The agreement is less good, as expected, when there are large defects in the ventilation scan, but the correlation between the two scans remains a useful one. This is not surprising because poorly ventilated areas are frequently poorly perfused. Of course, variations in the distribution of $\dot{V}/V_{A}$ interfere with the ability of ^{81}Kr^{m} infusion to portray the topography of blood flow accurately. Nevertheless, provided the distribution of inhaled ^{81}Kr^{m} does not alter, changes in regional perfusion can be followed by recording alternately the infusion and inhalation of ^{81}Kr^{m}.

In normal lungs, minute to minute changes in the distribution of pulmonary blood flow have been monitored. For example, Harf *et al.* (1978) showed in normal subjects that the apex doubled its share of total pulmonary flow (from 5 to 10%) within 20 seconds of the onset of mild (50 watt) exercise (see Fig. 12). Perfusion per unit alveolar volume cannot be obtained with ^{81}Kr^{m} infusion alone. Amis and colleagues (1978) have used the regional volume signal from $^{85}Kr^m$ gas equilibration to calculate perfusion per unit volume; the contribution of regional differences in $(\dot{V}_E/V_A+\lambda)$ to the perfusion image can also be allowed for.

By dividing the $^{81}Kr^m$ inhalation scan by the infusion scan, the topographical distribution of ventilation-perfusion $(\dot{V}_A/\dot{Q})$ ratios is obtained since the denominator in the equation $(\dot{V}_E/V_A+\lambda)$ is common to both measurements (assuming local homogeneity). Harf *et al.* (1978) have shown that the regional distribution of $\dot{V}_A/\dot{Q}$ measured with $^{81}Kr^m$ in normal subjects in the erect posture is similar to that found with other radionuclides ($C^{15}O_2$ and ^{133}Xe).

What are the relative merits of an injection of $^{99}Tc^m$-labelled microspheres and an infusion of $^{81}Kr^m$ for recording the distribution of pulmonary blood flow? $^{99}Tc^m$ is more convenient and because of its six hour half-life several images can be recorded in different views after a single injection. In addition, its distribution is independent of the pattern of ventilation, though this effect, for $^{81}Kr^m$ infusion, is not as serious as we feared (Ciofetta *et al.*, 1978a). On the other hand, it is better to measure perfusion with the same isotope and γ-energy as that used for ventilation. The short half-life of $^{81}Kr^m$ allows short-term changes in pulmonary blood flow distribution to be measured, and the radiation dose is much smaller than for technetium.

4.6 *Use in children*

The radiation dose associated with $^{81}Kr^m$ inhalation or infusion is extraordinarily low. M. Myers (personal communication) at Hammersmith has calculated a lung dose in adults of 0.6 mrad per 10^5 counts, rising to 13 mrad per 10^5 counts in infants. A normal study would not generally exceed 10^6 counts in adults and 3×10^5 in children. Thus, a $^{81}Kr^m$ study can be done without any appreciable radiation hazard in infants and children. In children who may have right to left cardiac shunts, the infusion of $^{81}Kr^m$ for regional pulmonary blood flow is safer than $^{99}Tc^m$-microspheres (though microsphere impaction in systemic tissues, in practice, does not seem to produce any untoward effects). The ease with which $^{81}Kr^m$ can be administered and recorded is an advantage where children are concerned. At Hammersmith and Great Ormond Street hospitals children of all ages (from four weeks old) have been studied without difficulty (Ciofetta, Gordon, Silverman and Fazio, personal communication). $^{81}Kr^m$ or ^{13}N lung scanning (Ciofetta *et al.*, 1978b; Ronchetti *et al.*, 1975b) is one of the few tests of pulmonary function which can be carried out in the age range 1–5 years because very little cooperation by the subject is required.

Although poorly ventilated areas are easily seen as defects on the $^{81}Kr^m$ image, a problem peculiar to children (and infants especially) is a very high alveolar ventilation per unit alveolar volume. This means that $\dot{V}_E/V_A$ frequently exceeds λ, so that the $^{81}Kr^m$ image begins to reflect alveolar volume and not ventilation (see Fig. 7). For this reason, Ciofetta *et al.* (1978b) have been recording the regional washout of inhaled or infused $^{81}Kr^m$ (Fig. 14) in order to distinguish volume from ventilation.

5. CONCLUSIONS

There are three main purposes for which short-life radioisotopes can contribute to pulmonary medicine: (a) to improve understanding of physiological mechanisms in the normal and diseased lung (see Figs. 3, 11, 12), (b) to aid the interpretation of simpler but more widely used tests of lung function (see Fig. 5), and (c) to help in diagnosis (see Fig. 10). Positron emitting isotopes whose use is limited to centres with immediate access to a cyclotron (except ^{11}C and ^{18}F) are unlikely ever to be widely used for their diagnostic value.

Because of the ^{81}Rb generator, $^{81}Kr^m$ is more widely available and its use embraces all three purposes. Nevertheless, and this may come as a surprise to radiologists and specialists in nuclear medicine, the value of $^{81}Kr^m$ as a diagnostic aid is small compared

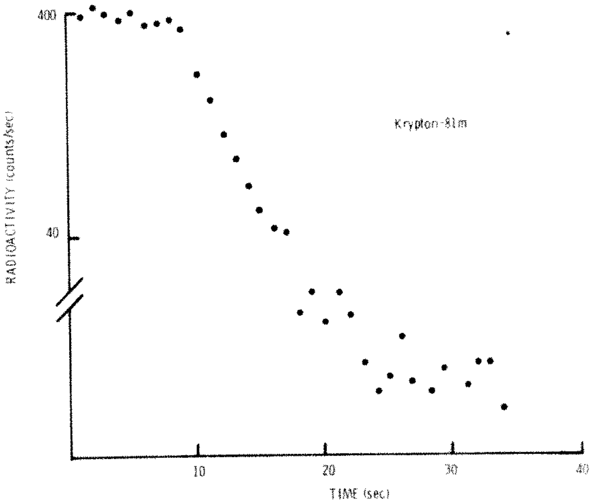

Fig. 14.

Whole lung clearance of $^{81}Kr^m$ after steady-state inhalation in a child aged two years. Ventilation per unit volume $(\dot{V}_E/V_A)$ calculated from the initial slope of the disappearance curve, is 10.0 min^{-1} (normal value in adults 1.0–2.0 min^{-1}).

with its potential in areas (a)—mechanisms in disease—and (b)—interpretation of simple measurements. For example, $^{81}Kr^m$ as a diagnostic agent is really only of value in two areas, preoperative assessment and pulmonary embolism. Indeed, many would maintain that the combination of a technetium perfusion scan and (in difficult cases) angiography is sufficient to reach a firm diagnosis of pulmonary embolism. $^{81}Kr^m$ inhalation should be of much greater benefit in the assessment of, for example, (1) effects of physiotherapy in post-operative management, (2) the best route of administration of bronchodilator drugs, (3) changes in ventilation distribution during sleep or anaesthesia, and (4) interpretation of changes in overall pulmonary function in asthma.

The temptation is to regard $^{81}Kr^m$ only as an improvement on ^{133}Xe. It is much more than that. For the first time, minute to minute changes in regional pulmonary function can be assessed and the immediate response to therapy measured. There are problems of quantitation, but section 4.4 proposes some solutions. The krypton ventilation scan alone gives relative information, comparing one region with another; it should always be interpreted with knowledge of the results of overall pulmonary function tests and the chest radiograph.

5.1 *Future prospects*

Interest in the use of positron emitters will be considerably enhanced with the advent of the positron camera. With the technique of positron emission tomography, the distribution of radioactivity in the thorax can be reconstructed in three dimensions (Chesler *et al.*, 1975). Thus, the errors caused by radioactivity in the chest wall and attenuation within the lung itself will be removed. In addition, quantitation will be more accurate, the aim being to relate, by external counting, concentrations of tracer radioactivity in lung tissue to their concentrations in inspired air (the trachea) or in blood (right or left ventricle). There is also likely to be increasing interest in the regional uptake and metabolism of organic compounds (amines and sugars labelled with ^{13}N, ^{11}C or ^{18}F), ammonia ($^{13}NH_3$) and even larger molecules such as immunoglobulins, lipoproteins and pharmacological substances. The handling of amines (^{11}C-octylamine and ^{11}C-5-hydroxytryptamine) by the lung has been studied (Gallagher *et al.*, 1977).

The krypton ventilation scan will continue to assist in the diagnosis of pulmonary vascular obstruction. Hopefully, it will be used much more as a research tool to identify patho-physiological mechanisms and to aid in the interpretation of the simpler tests of function. Publication of the results and experience of users outside Hammersmith is awaited with interest.

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REFERENCES

Amis, T. C., Ciofetta, G., Clark, J. C., Hughes, J. M. B., Jones, Hazel A., and Pratt, T. A., 1977, Effect of posture on distribution of pulmonary ventilation and perfusion studied with $^{81}Kr^m$ and $^{85}Kr^m$. *Journal of Physiology, 272*, 76–77.

1978. Use of $^{81}Kr^m$ and $^{85}Kr^m$ for measurement of ventilation and perfusion distribution within the lungs. In *Clinical and Experimental Applications of Krypton-81m*, London. British Journal of Radiology. Special report No. 15, pp. 52–59.

Binswanger, R. O., Rosler, H., Noelpp, U., Matter, L., and Haertel, M., 1978. The bedside determination of extravascular lung water. *European Journal of Nuclear Medicine, 3*, 109–114.

Chesler, D. A., Hales, C., Hnatowich, D. J., and Hoop, B., 1975. Three-dimensional reconstruction of lung perfusion image with positron detection. *Journal of Nuclear Medicine, 16*, 80–82.

Chinard, F. P., 1975. Estimation of extravascular lung water by indicator-dilution techniques. *Circulation Research, 37*, 137–145.

Ciofetta, G., Pratt, T. A., and Hughes, J. M. B., 1978a. Regional pulmonary perfusion assessed with continuous intravenous infusion of $^{81}Kr^m$: a comparison with $^{99}TC^m$-macroaggregates ($^{99}Tc^m$-HAM). *Journal of Nuclear Medicine, 19*, 1126–1130.

Ciofetta, G., Silverman, M., and Hughes, J. M. B., 1978b. Use of krypton-81m for measuring regional lung function in children. *Clinical Science and Molecular Medicine, 55*, 24P.

Clark, J. C., and Buckingham, P. D., 1975. In *Short-lived radioactive gases for clinical use* (Butterworths, London).

Dollery, C. T., Heimburg, P., and Hugh-Jones, P., 1962. The relationship between blood flow and clearance rate of radioactive carbon dioxide and oxygen in normal and oedematous lungs. *Journal of Physiology, 162*, 93–104.

Dollery, C. T., and Matthews, C. M. E., 1971. The influence of pulmonary oedema on the distribution and measurement of regional pulmonary blood flow with $C^{15}O_2$. In *Central Haemodynamics and Gas Exchange*. Ed. C. Giuntini, chap. 17, pp. 251–262 (Minerva Medica, Torino).

Eiser, N. M., Jones, Hazel A., and Hughes, J. M. B., 1977. Effect of 30% oxygen on local matching of perfusion and ventilation in chronic airways obstruction. *Clinical Science and Molecular Medicine, 53*, 387–395.

Ewan, P. W., Jones, H. A., Nosil, M., Obdrzalek, J., and Hughes, J. M. B., 1978. Uneven perfusion and ventilation within lung regions studied with nitrogen-13. *Respiration Physiology*, *34*, 45–49.

Ewan, P. W., Jones, H. A., Rhodes, C. G., and Hughes, J. M. B., 1976. Detection of intrapulmonary haemorrhage with carbon monoxide uptake: application in Goodpasture's syndrome. *New England Journal of Medicine*, *295*, 1391–1396.

Fazio, F., Jones, T., MacArthur, C. G. C., Rhodes, C. G., Steiner, R. E. S., and Hughes, J. M. B., 1976. Measurement of regional pulmonary oedema in man using radioactive water ($H_2{}^{15}O$). *British Journal of Radiology*, *49*, 393–397.

Fazio, F., and Jones, T., 1975. Assessment of regional ventilation by continuous inhalation of radioactive krypton-81m. *British Medical Journal*, *3*, 673–676.

Fazio, F., Lavender, J. P., and Steiner, R. E., 1978. $^{81}Kr^m$ ventilation and $^{99}Tc^m$ perfusion scans in chest disease. Comparison with standard radiographs. *American Journal of Roentgenology*, *130*, 421–428.

Gallagher, B., Christman, D., Fowler, J., MacGregor, R., Wolf, A. P., Som, P., Ansari, A. N., and Atkins, H., 1977. Radioisotope scintigraphy for the study of dynamics of amine regulation by the lung. *Chest*, *71*, 282–284S.

Godfrey, S., and Mackenzie, S., 1977. The place of radioisotopic lung function studies in paediatrics. *Archives of Diseases in Childhood*, *52*, 859–864.

Grant, B. J. B., Jones, H. A., and Hughes, J. M. B., 1974. Sequence of regional filling during a tidal breath in man. *Journal of Applied Physiology*, *37*, 158–165.

Hales, C. A., Gibbons, R., Burnham, C., and Kazemi, H., 1976. Determinants of regional distribution of a bolus inhaled from residual volume. *Journal of Applied Physiology*, *41*, 400–408.

Harf, A., Pratt, T., and Hughes, J. M. B., 1978. Regional distribution of $\dot{V}_A/\dot{Q}$ in man at rest and with exercise measured with krypton-81m. *Journal of Applied Physiology*, *44*, 115–123.

Heather, J. D., Hughes, J. M. B., MacArthur, C. G. C., Rhodes, C. G., and Swinburne, A. J., 1978. Assessment of lung water with inhaled $C^{15}O_2$ and injected $H_2{}^{15}O$. *Journal of Physiology*, *284*, 103–104.

Hughes, J. M. B., 1977. Pulmonary oedema. In *Regional differences in the lung*. Ed. J. B. West, pp. 381–419 (Academic Press, New York).

Hughes, J. M. B., Gardiner, I. G., and Ciofetta, G., 1978. Induced broncho-constriction. In *Clinical and Experimental Applications of Krypton-81m*. Special report 15, pp. 125–129 (British Journal of Radiology, London).

Jones, T., Clark, J. C., Hughes, J. M. B., and Rosenzweig, D. Y., 1970. $^{81}Kr^m$ generator and its uses in cardiopulmonary studies using a scintillation camera. *Journal of Nuclear Medicine*, *11*, 118–124.

Jones, T., Fazio, F., and Hughes, J. M. B., 1975. Assessment of regional lung ventilation by the continuous inhalation of krypton-81m: a new technique. *Clinical Science and Molecular Medicine*, *49*, 8–9.

Jones, T., Jones, Hazel A., Rhodes, C. G., Buckingham, P. D., and Hughes, J. M. B., 1976. Distribution of extravascular fluid volumes in isolated perfused lungs measured with $H_2{}^{15}O$. *Journal of Clinical Investigation*, *57*, 706–713.

Jones, T., Clark, J. C., Rhodes, C. G., Heather, J., and Tofts, P., 1978. Combined use of krypton-81m and 85m in ventilation studies. In *Clinical and Experimental Applications of Krypton-81m*, Special Report 15, 46–51 (British Journal of Radiology, London).

Lavender, J. P., 1978. In *Clinical and Experimental Applications of Krypton-81m*, Special report 15, (British Journal of Radiology, London).

Lipscomb, D. J., and Pride, N. B., 1977. Ventilation and perfusion scans in the preoperative assessment of bronchial carcinoma. *Thorax*, *32*, 720–725.

Matthews, C. M. E., and Dollery, C. T., 1965. Interpretation of ^{133}Xe lung wash-in and wash-out curves using an analogue computer. *Clinical Science*, *28*, 573–590.

McKenzie, S. A., MacArthur, C. G. C., Godfrey, S. and Hallidie-Smith, K. A., 1977, Hypertensive pulmonary vascular disease in children. Detection by radioactive nitrogen (^{13}N) inhalation and injection. *British Heart Journal*, *39*, 860–871.

Nichols, A. B., Cochavi, S., Hales, C. A., Strauss, H. W., McKusick, K. A., Waltman, A. C., and Beller, G. A., 1978. Scintigraphic detection of pulmonary emboli by serial positron imaging of inhaled ^{15}O-labelled carbon dioxide. *New England Journal of Medicine*, *229*, 279–284.

Pande, J. N., Lipscomb, D. J., Forse, G., Jones, T., and Hughes, J. M. B., 1976. Regional differences in carbon monoxide uptake in the lung. In *Distribution des échanges gazeux pulmonaires*, *51*, pp. 169–174 (Editions INSERM, Paris).

Ronchetti, R., Ewan, P. W., Jones, T., and Hughes, J. M. B., 1975a. Use of ^{13}N for regional clearance curves compared with ^{133}Xe. *Bulletin Europeen de Physio-pathologie Respiratoire*, *11*, 124–125.

Ronchetti, R., Stocks, J., Freedman, N., Glass, H., and Godfrey S., 1975b. The clinical application of regional lung function studies in infants and small children using ^{13}N. *Archive of Diseases in Childhood*, *50*, 595–603.

Rosenzweig, D. Y., Hughes, J. M. B., and Jones, T., 1969/70. Uneven ventilation within and between regions of the normal lung measured with nitrogen-13. *Respiration Physiology*, *8*, 86–97.

Schmidt-Nowara, W. W., Hoop, B., and Kazemi, H., 1973. Role of pulmonary blood flow in removal of gaseous isotopes from the lung. *Journal of Applied Physiology*, *35*, 655–661.

Suda, Y., Martin, C. J., and Young, A. C., 1970. Regional dispersion of volume to ventilation ratios in the lung of man. *Journal of Applied Physiology*, *29*, 480–485.

Taplin, G. V., Chopra, S. K., MacDonald, N. S., and Elam, D., 1976. Imaging small pulmonary ischaemic lesion after radioactive carbon monoxide inhalation. *Journal of Nuclear Medicine*, *17*, 866–871.

West J. B., and Dollery, C. T., 1960. Distribution of blood flow and ventilation-perfusion ratio in the lung measured with radioactive CO_2. *Journal of Applied Physiology*, *15*, 405–410.

1962. Uptake of oxygen-15 labelled CO_2 compared with carbon-11-labelled CO_2 in the lung. *Journal of Applied Physiology*, *17*, 9–13.

West, J. B., Holland, R. A. B., Dollery, C. T., and Matthews, C. M. E., 1962. Interpretation of radioactive gas clearance rates in the lung. *Journal of Applied Physiology*, *17*, 14–20

West, J. B., 1977. *Regional differences in the Lung*. (Academic Press Inc., New York).

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Measurement of regional cerebral blood volume using the EMI 1010 scanner

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ABSTRACT

Regional cerebral blood volume (rCBV) was measured in 14 patients with normal CT scans. An EMI CT 1010 scanner was used in combination with a computer subtraction technique. The mean CBV in the cortex was 5.0 ml/100 ml of tissue and 2.2 in the white matter. Regional differences were not significant and no difference was found between the right and left hemispheres.

Regional cerebral blood volume (rCBV) has been measured using computer tomography (Ladurner *et al.*, 1976) combined with a computer subtraction technique (Zilkha *et al.*, 1976). The present paper describes rCBV measurements in 14 patients with normal scans using the CT 1010 scanner. Its lower stability is more than compensated by the considerably shorter scanning time and better resolution than the first generation EMI scanner; the effect is an improvement in CBV methodology.

METHODS

Fourteen patients were studied (11 women and three men), the clinical details of whom are shown in Table I. All patients were right handed as far as could be assessed by questioning. Only patients who had no neurological deficit and a normal CT scan were included in the series. The majority of the patients were receiving treatment for grand mal epilepsy. Psychiatric findings were negative except for two patients with a neurotic depression.

An EMI CT 1010 scanner was used with a scanning time of 60 seconds. Two cuts were made 43 and 56 mm above the orbitomeatal line and repeated after injection of 150 ml of megluminamidotrizoate (Urovist R) over approximately one minute into an arm vein while the patient remained in an identical position. Blood samples were taken from the opposite arm vein during both scans to determine its spectrophotometric absorption (Ladurner 1979). This enabled the level of megluminamidotrizoate in the blood (in mg/100 ml of plasma) to be estimated using a method described by Purkiss *et al.* (1968) for sodium diatrizoate. Capillary blood samples were taken simultaneously from a finger tip to determine the haematocrit and the PCO_2.

rCBV was calculated as described in a previous paper (Zilkha *et al.*, 1976) and will therefore only be summarized here. The CT data was processed by a Varian 73 computer equipped with 12K 16-bit words of core memory, a cartridge disc unit, a

TABLE I

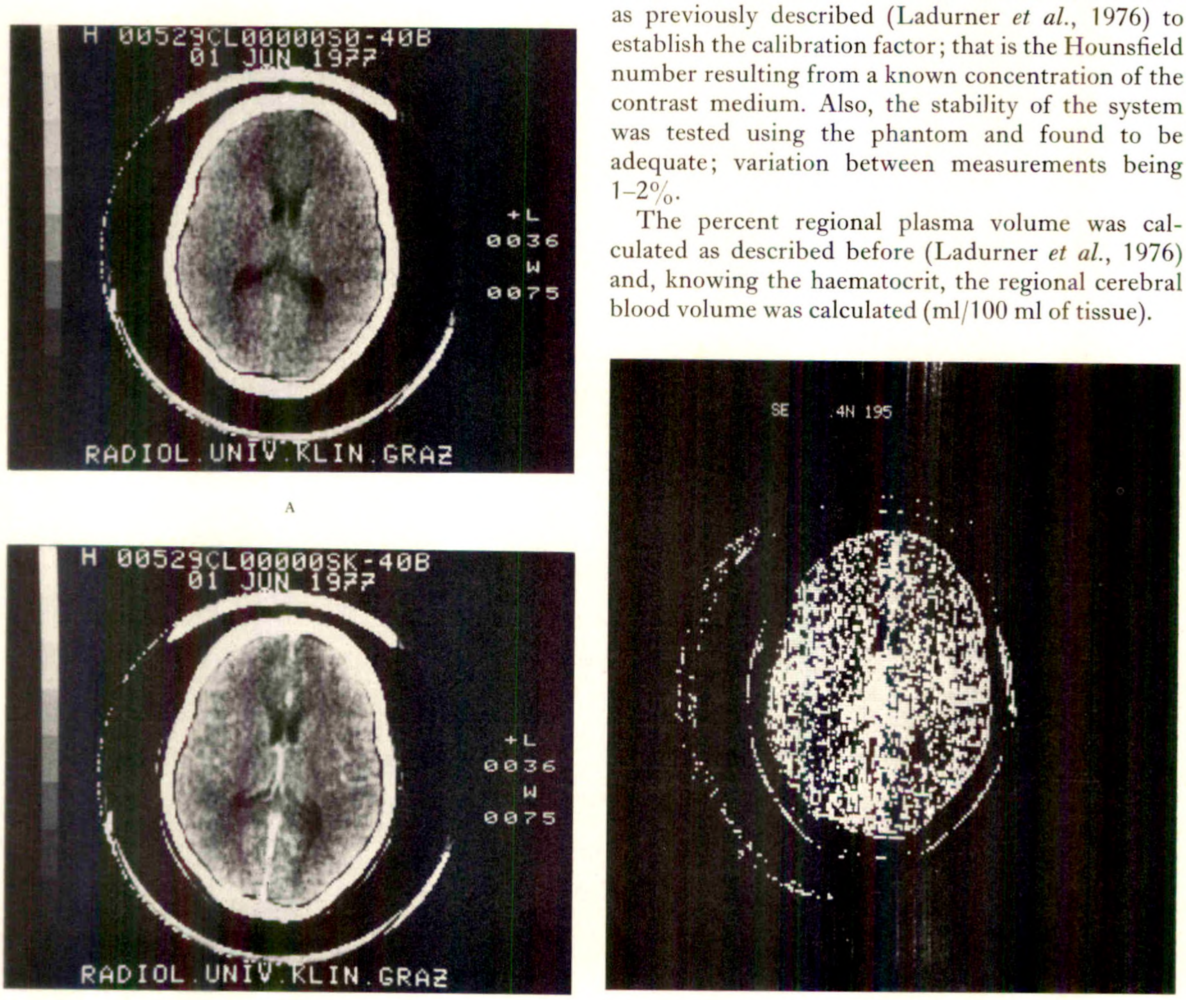
PATIENT DATA, CONTRAST MEDIUM LEVELS, HAEMATOCRIT AND $PcCO_2$

Patient no.	Age (yr)	Final diagnosis	Megluminamido-trizoate (mg/100 ml)	Haematocrit		$PcCO_2$ (mm Hg)	
				Scan 1	Scan 2	Scan 1	Scan 2
1	16	Epilepsy	963	36	31	23	23
2	45	Epilepsy	1529	34	27	31	30
3	23	Epilepsy	1311	40	33	35	33
4	17	Epilepsy	1821	37	31	39	38
5	20	Epilepsy	931	43	38	35	33
6	51	Depression	1676	40	33	44	42
7	32	Epilepsy	1081	37	32	39	42
8	54	Epilepsy	782	41	37	36	33
9	16	Epilepsy	1035	42	33	36	36
10	22	Depression	1195	48	33	39	32
11	32	Epilepsy	977	40	37	35	44
12	37	Epilepsy	1270	42	35	36	32
13	24	Epilepsy	1242	41	38	34	38
14	63	Neuralgia	1531	37	30	46	39
Mean	32		1238	40	33	36	35
SD			307	4	3	5	6

seven-track IBM compatible magnetic tape unit, a Tektronix 4010 terminal and a teletype. The outlines of the patient's skull obtained from the CT scans were displayed on the Tektronix screen and, in this series, good superimposition was achieved in every case without correction being necessary, showing that all 14 patients had remained completely still. The computer subtracted the pre-injection from the post-injection scan and the resultant subtracted picture was displayed on the screen. From this picture areas were selected using the cross hairs on the screen of the terminal and the computer then calculated the mean difference in Hounsfield number for that area. The mean value, its SD, SE and number of EMI matrix cells were shown on the screen and printed out by the teletype. The CT pictures obtained were of a quality such that in all cases grey and white matter were distinguishable. It was therefore possible to select areas which consisted mainly of grey matter or white matter and this was done for both right and left hemispheres in the frontal, temporal and occipital regions, together with an overall measurement for grey and white matter respectively. Results from the two adjacent cuts were combined to give a mean. Values were also obtained for the basal ganglion when it could be well visualized. Artefacts in the CT pictures were few but, when present, were avoided, as were very dense areas due to contrast medium in large vessels (Fig. 1).

Phantom studies were carried out on the CT 1010 as previously described (Ladurner *et al.*, 1976) to establish the calibration factor; that is the Hounsfield number resulting from a known concentration of the contrast medium. Also, the stability of the system was tested using the phantom and found to be adequate; variation between measurements being 1–2%.

The percent regional plasma volume was calculated as described before (Ladurner *et al.*, 1976) and, knowing the haematocrit, the regional cerebral blood volume was calculated (ml/100 ml of tissue).



A

B

C

FIG. 1.

Figure 1A and 1B shows the same cut before and after injection of 150 ml megluminamidotrizoate respectively. Note filling of large vessels centrally. Figure 1C is the subtracted picture of 1A from 1B.

RESULTS

Table I shows the level of megluminamidotrizoate in the blood, the haematocrits for the first and second scans and the corresponding capillary PCO_2 levels. The concentration of megluminamidotrizoate varied between 782 and 1821 mg/100 ml with a mean value of 1238 mg/100 ml. The average fall in haematocrit between the first and second scan was 17%. Capillary PCO_2 was not significantly different for the two scans and had a mean value of 36 and 35 mm Hg respectively.

The average blood volume in the cortex (Table II) was 5.0 on the right and 5.0 ml/100 ml of tissue on the left. The highest regional blood volume was found in the temporal lobes with 6.3 in the right and 6.2 ml/100 ml tissue in the left. Table III shows the mean blood volume values in the basal ganglion separated into the caudate nucleus and the thalamus. The values are similar to those found in the cortex and again show no significant difference in the sides.

rCBV in the white matter is shown in Table IV with an average of 2.2 for the right side and 2.3 ml/100 ml tissue for the left. Again, there was no significant difference either between sides or regions, though the temporal regions had the highest values. The difference between CBV in the white matter and both cortex and basal ganglion was highly significant ($P<0.001$), the value in white matter being nearly a third of that in grey matter.

TABLE II

rCBV IN MAINLY GREY MATTER (ml/100 ml)

	Right	Left
Frontal	5.6 (2.6)	5.8 (2.2)
Temporal	6.3 (2.1)	6.2 (2.4)
Occipital	4.9 (1.7)	4.1 (1.2)
Hemisphere	5.0 (1.5)	5.0 (1.5)

TABLE III

CBV IN THE BASAL GANGLION (ml/100 ml)

	Right	Left
Caudate nucleus	5.9 (2.5)	6.7 (2.3)
Thalamus	5.5 (3.5)	4.4 (1.8)

TABLE IV

rCBV IN THE WHITE MATTER (ml/100 ml)

	Right	Left
Frontal	2.3 (0.9)	2.4 (0.8)
Temporal	2.7 (1.1)	2.7 (0.9)
Occipital	2.1 (0.6)	2.1 (0.7)
Hemisphere	2.2 (0.7)	2.3 (0.6)

DISCUSSION

CBV can be expressed in two ways; the first being in ml/100 gm tissue, when CBV is calculated from cerebral blood flow (ml/100 gm/min), as in the measurements by Mathew *et al.*, (1975). Grub *et al.* (1973) have also the same units in their CBV estimations involving a radio fluorescent technique. The other way of expressing CBV emphasizes blood volume as a percentage of cerebral tissue volume (ml/100 ml tissue), as we have, and Zilkha *et al.* (1976) in previous studies using CT. Reivich *et al.* (1974) also used the same in their estimations of CBV using Tc^{99} labelled erythrocytes. The quantitative difference between ml/100 gm and ml/100 ml is insignificant, but nevertheless worth bearing in mind, if only for purposes of clarification.

The cortical results from the present study of rCBV in fourteen patients with normal CT scans are basically similar to those found previously (Zilkha *et al.*, 1976) despite the use of different contrast media, a different scanner and a considerably larger and younger group of patients. This in itself is a ground for reasonable confidence in the methodology, and the suitability of the CT 1010 scanner for rCBV estimation.

The contrast medium used in this series was well tolerated even when 150 ml were injected relatively rapidly, the patients being able to remain very still since discomfort was minimal. Plasma levels of contrast medium were higher in this study but, because megluminamidotrizoate has a lower iodine content (306 mg/ml as opposed to 420 mg/ml in Conray), the change in EMI number in the brain due to contrast medium was only slightly raised (2.5 EMI numbers as opposed to 2.2 EMI numbers in the previous investigation). Nevertheless this slight increase together with the better tolerance would indicate that megluminamidotrizoate has a distinct advantage over Conray for CBV measurements.

In the CT 1010 scanner the head positioning is easier without the presence of a water bag and this, together with the faster scan results in less discomfort for the patient and therefore fewer movement artefacts. Where precise subtraction is required, as in rCBV measurements, movement artefacts are particularly to be avoided and this was possible in all 14 patients.

The higher resolution allows better visualization of anatomical features, in particular distinguishing between grey and white matter and therefore making the measurement of CBV possible in each separately. Large vessels containing contrast medium can also be well seen and avoided in the areas selected for measurement. A further advantage of the faster scanning period is that it makes dynamic studies possible, such as the investigation of the effect of hyperventilation on rCBV.

We cannot be certain whether the lack of any significant difference between the two hemispheres in the present study is evidence of greater or lesser accuracy of measurement than in the paper of Zilkha *et al.* (1976). Previously we had shown a higher regional CBV on the left—a finding also reported by Grubb *et al.* (1978).

We have demonstrated the suitability of the CT 1010 for measuring rCBV; the method has been improved by two major modifications. The first is a considerably faster scanning speed and the second is the use of a different contrast medium. In the future both these features can be further improved, with scanning periods of as little as three seconds and the development of new contrast media.

REFERENCES

Grubb, R. L., Phelps, M. E., and Ter-Pogossian, M. M., 1973. Regional cerebral blood volume in humans. *Archives of Neurology*, *28*, 38–44.

Grubb, R. L., Raichle, M. E., Higgins, C. S., and Etchling, J. O., 1978. Measurement of regional cerebral blood volume by emission tomography. *Annals of Neurology*, *4*, 322–328.

Ladurner, G., Zilkha, E., Iliff, L. D., Du Boulay, G. H., and Marshall, J., 1976. Measurement of regional cerebral blood volume by computerized axial tomography. *Journal of Neurology, Neurosurgery and Psychiatry*, *39*, 152–158.

Ladurner, G., 1979. Die Bestimmung des cerebralen Blutvolumens mit der Computertomographie in grauer und weßer Substanz. *Fortschritte der Neurologie und Psychiatrie.* (In Press).

Mathew, N. T., Meyer, J. S., and Ott, E., 1975. Increased cerebral blood-volume in benign intracranial hypertension. *Neurology*, *25*, 646–649.

Purkiss, P., Lane, R. D., Cattel, W. R., Kelsey Fry, I., and Spencer, A. G., 1968. Estimation of sodium diatrizoate by absorption spectrophotometry. *Investigative Radiology*, *3*, 271–274.

Reivich, M., Kuhl, D. E., and Nyary, I., 1974. Measurement of local cerebral blood volume in three dimensions in man. *Neurology* (Minneap.), *24*, 389.

Zilkha, E., Ladurner, G., Iliff, L. D., Du Boulay, G. H., and Marshall, J., 1976. Computer subtraction in regional cerebral blood-volume measurements using the EMI scanner. *British Journal of Radiology*, *49*, 330–334.

Book review

Ultrasound in Gynecology and Obstetrics. By S. N. Hassani, pp. xx + 182, illus., 1978 (Springer Verlag, Berlin) DM49.60/ $24.80.
ISBN 3-540-90260-0.

This is a moderately large and moderately expensive book which contains a wealth of illustrations and initially appears rather promising. When reading the book however, it is evident that the contents have been spread fairly thinly across the pages, and a significant proportion of the book is taken up by two forewords, a preface, an introduction and a small acknowledgment. Twelve pages elapse before one arrives at the first chapter. This chapter consumes a further 38 pages discussing the principles of ultrasound, as has been done in almost every other book, and must surely by now be entirely superfluous. The second chapter concerns the value of ultrasound in gynaecology, and occupies only 30 of the book's 190 pages. A further 60 pages is devoted to obstetrics and thus just under half of this book concerns the topic presented in the title. The final chapter is the second longest in the book, and concerns "ultrasonography of gynaecologically and obstetrically related medical and surgical disorders". This chapter in fact contains a discussion of the value of ultrasound in the liver, gall-bladder, aorta, spleen, thyroid, kidney, heart, etc, and much of the material presented has no obvious connection with either obstetrics or gynaecology, and is of little if any relevance in such a book.

Dr. Hassani lives and works in America and I found much of his terminology rather unacceptable. He discusses a a phenomenon which he terms "three dimensional conceptualization" which I thought likely to be relevant in a book on obstetrics, but discover that this is in fact a thought process on behalf of the ultrasound operator. I also note that he uses the term B mode to mean bistable display, though this is not its generally accepted meaning, and he has also coined his own words such as sonolaparotomy, sonoanatomy, and sonofluoroscopy. The latter of these apparently does not necessarily mean real time ultrasound. The author also has some unusual ideas concerning anatomy and physiology. He shows us a picture of a partially filled urinary bladder with a non-specific echo pattern at its fundus which he claims to be "the unfilled portion of the bladder!" He also includes a transverse scan of the fetal head in which there are multiple curved reverberation artefacts from the anterior skull wall. He tells us that occasionally the mid-line echo appears as a curve, but this is still a valid image for measurement of the BPD. It most certainly is not, and such statements will only mislead unskilled and inexperienced operators. The author should read page 23 of his chapter on the principles of ultrasound where he discusses the occurrence of such reverberations.

While many of the illustrations included in the book are of fairly good quality, a significant proportion are rather poor and a small minority are extremely bad.

There are now many fairly good books available on the uses of ultrasound in obstetrics and gynaecology and this book compares unfavourably with most of them, and therefore cannot be recommended.

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Diagnosis of diaphragmatic tears

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ABSTRACT

Twenty-five cases of torn diaphragm with herniation of abdominal contents and 22 cases without herniation were studied. Without herniation, the chest radiograph was in most cases normal or almost so, the remainder showing haemothorax or pneumothorax attributable to associated lung or rib injury. With herniation, however, the chest radiograph was infrequently normal and a substantial number showed basal abnormality directly due to herniated viscera. The appearances were still, however, non-specific and led to a number of preliminary misdiagnoses and therefore diagnostic delays. The herniated bowel can flatten out beneath the lung base to resemble merely a mildly elevated hemidiaphragm (the "pseudo-diaphragm effect").

Torn hemidiaphragm is a frequently forgotten diagnosis, but is of great importance because of hernial bleeding or strangulation. The peritoneopleural pressure gradient eventually produces herniation and this is usually diagnosable by barium study of stomach and colon. Small bowel studies are probably unnecessary. The limbs of the herniated loop are pinched together as they pass through the tear, sometimes severely enough to obstruct the barium. Insufflated air may get through into an apparently obstructed hernia. Because it is a "blind alley", the herniated gastric fundus will not produce these typical appearances and will be missed unless one looks for the "amputated fundus" sign.

Immediately following injury, normal barium studies do not necessarily indicate that there is no tear because there may not have been time for herniation to occur. The only available signs may therefore be the presence of a pneumoperitoneum or of intra-abdominal visceral injury following a downward stab to the lower chest, or of pneumothorax following abdominal injury. Diagnostic pneumoperitoneum may have a place.

A left-sided predominance in all series is probably due to the liver cushioning the right hemidiaphragm from rupture in abdomino-pelvic crush injuries and also preventing bowel from herniating through established stab wounds.

There is a need for clinicians and radiologists to be more aware of the torn diaphragm. At present diagnosis is often missed or delayed. (Carter *et al.*, 1951; Hill, 1972; Tan *et al.*, 1973; Gourin and Garzon, 1974). This is due to the normal or non-specific appearance of plain radiographs even in the presence of herniation; attention may be diverted by other injuries and to its relative rarity in blunt and penetrating thoraco-abdominal trauma. In areas where stabbings, bullet-wounds and road accidents all contribute to thoraco-abdominal injury, the torn diaphragm is not at all rare and its importance lies in the seriousness of the complications of bowel herniation through the tear. There is a mortality of up to 30% in those patients in whom diagnostic delay has resulted in strangulation of herniated bowel (Grage *et al.*, 1969; Gourin and Garzon, 1974). The most important factor in making the diagnosis is a high index of suspicion in all cases of blunt or penetrating injury to the lower chest or upper abdomen, or of crush injury to the abdomen or pelvis.

MATERIAL

During the three-year period 1974 to 1976, 39 patients with ruptured diaphragm were treated at Groote Schuur Hospital. The departmental film library also contained the radiographs of eight further patients treated during the period 1966 to 1973. Our study was a mainly retrospective analysis of clinical and radiological findings.

CLINICAL BACKGROUND

Eleven cases were due to motor vehicle accidents, 30 to stab wounds of the lower chest, two to stab wounds of the upper abdomen, one to assault with a stick and two to bullet wounds. There was one case of unknown, possibly forgotten trauma.

Twenty-nine patients had some abdominal pain and/or tenderness and four had features of intestinal obstruction. Fourteen had haemo- and/or pneumo-thoraces. Thirty-six patients presented within 24 hours of their trauma and a further five within a week; in the remaining six it took between two months and 30 years for the torn diaphragm to come to medical notice.

The rupture was left-sided in 40 cases and right-sided in seven; no patient had bilateral ruptures. The size of the rupture was not recorded in 27 cases. Of those recorded, the 16 due to stab wounds were all less than 50 mm wide and the four due to motor vehicle accidents were all greater than 80 mm wide. The other seven due to motor vehicle accidents were all described as large or massive.

Twenty-five cases were associated with herniation of abdominal viscera. In the case of stab wounds, only one organ was ever involved, but motor vehicle accidents always had two or more organs due to the greater size of the defect. None of the right-sided ruptures were associated with herniation. Hernial content varied: the colon (13) and stomach (11) were common; the rest included omentum (eight), small bowel (four), spleen (three) and liver (one).

A number of associated injuries were present, many creating the indications for laparotomy in the acute cases. Eighteen cases (16 due to stab wounds) had ruptured spleens. Eleven patients (9 due to stab wounds) had ruptured livers. Five of the 11 motor vehicle accident victims had a fractured pelvis. Other injuries included perforated stomach or bowel in 11 patients, one case each of ruptured kidney, pancreas and adrenal, skeletal fractures in four and a false aneurysm of the thoracic aorta in another. Two patients died—one from brain damage and the other from intra-abdominal bleeding due to multiple liver lacerations.

RADIOLOGICAL FINDINGS AND DISCUSSION

Tears with herniation

Spontaneous healing of a tear is unlikely because the peritoneopleural pressure-gradient favours the upward movement of abdominal contents into the chest, thus keeping the tear open and causing herniation (Gourin and Garzon, 1974). This herniation may be immediate or delayed by hours, days or years especially if the tear is small (Carter *et al.*, 1951).

Symptoms of herniation include: pain in the upper abdomen or lower chest which may be referred to the shoulder (Efron and Hyde, 1967) or be increased by bending or eating; episodes of obstruction; bleeding, which may be slow and occult or acute; and a variety of milder symptoms depending on which part of the bowel has herniated. These symptoms may mimic myocardial infarction, peptic ulcer or gall stone disease (Lernau *et al.*, 1974).

Any of the above symptoms in patients with previous blunt or open trauma to the abdomen or lower chest, together with a basal abnormality on the chest radiograph, should alert one to the possibility of herniation. It is especially so if radiographs at the time of the trauma showed any evidence of diaphragmatic elevation or basal haemothorax.

In the presence of herniation plain films are generally more abnormal than in cases without herniation. Of the 25 patients with herniation, only two had normal chest radiographs; 13 showed some degree of haemothorax or haemopneumothorax obscuring the base; while ten had abnormal patterns at the left base due directly to the herniated bowel, but so non-specific in appearance that they frequently gave rise to preliminary misdiagnosis (Figs. 1–7). In those patients whose radiographs showed no abnormality or only pneumothorax or haemothorax, operation revealed only small hernias and in four the hernias consisted only of omentum.

The herniated portion of stomach or colon can flatten out beneath the lung base and mimic a mildly elevated hemidiaphragm (Hill, 1972; Carter *et al.*, 1951). This is the pseudodiaphragm effect (Figs. 5A, 6C). On the other hand, when a large part of the stomach has herniated, it can distend upward even further than in Figs. 2 and 3 to occupy most of the hemithorax and displace the mediastinum to the other side. It may then resemble a tension pneumothorax if the herniated bowel is air-filled, or a massive

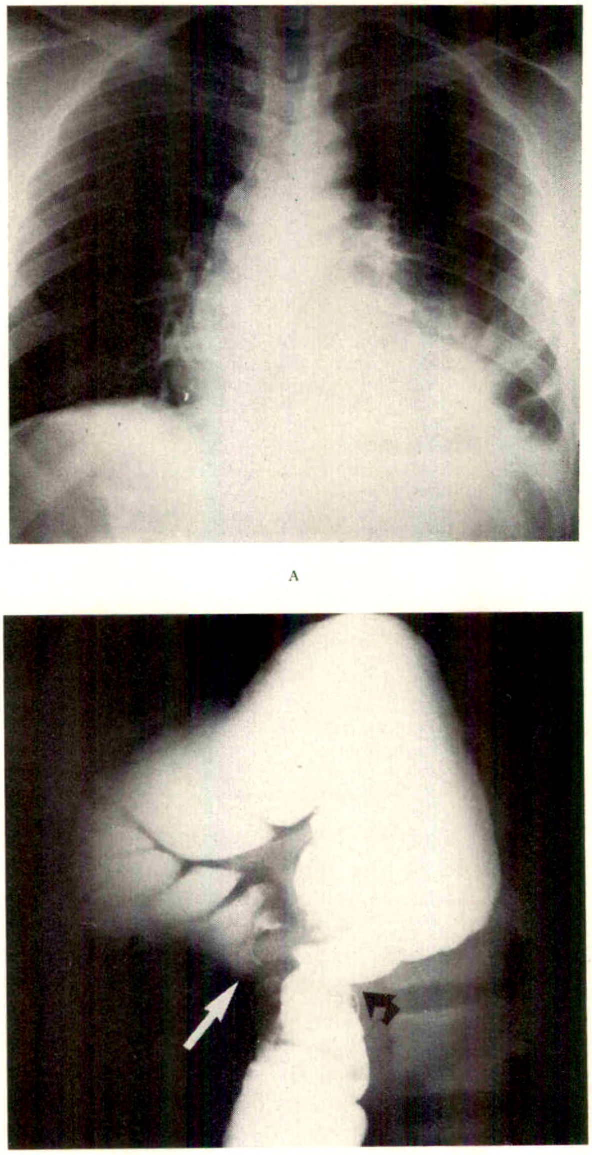


FIG. 1.

♂ Stab wound left axilla.

(A) Erect film shows an abnormal gas pattern at the left base.

(B) Barium enema. Herniated transverse colon with obstruction of proximal limb (white arrow) and narrowed distal limb (black arrow) is shown.

pleural effusion if it is fluid-filled. Other mistaken diagnoses in this and other series when gas-filled bowel has been present above the diaphragm, have been total or segmental eventration (Fig. 3), acute gastric dilatation (Fig. 3), gastric volvulus, phrenic nerve palsy, subphrenic abscess, loculated pneumothorax (Fig. 1A), traumatic pneumatocoele (Fig. 6A)

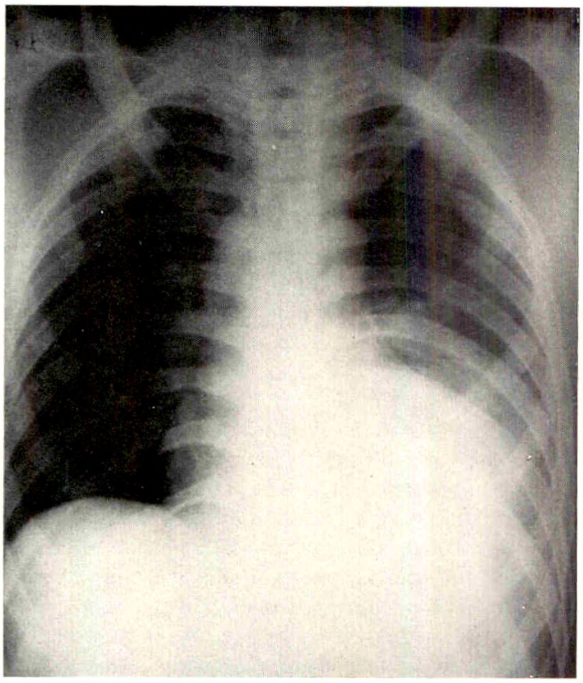


FIG. 2.

♂ R.T.A. Unconscious.
Chest X-ray—supine. There is homogenous opacification at the left base. Autopsy confirmed herniated stomach.

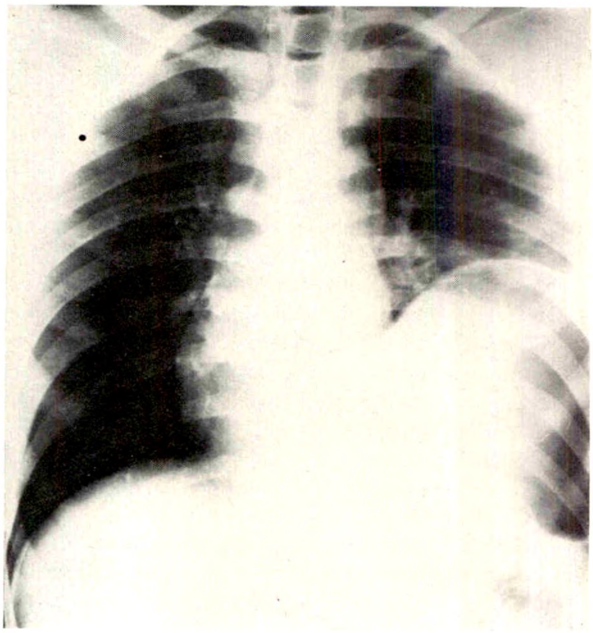
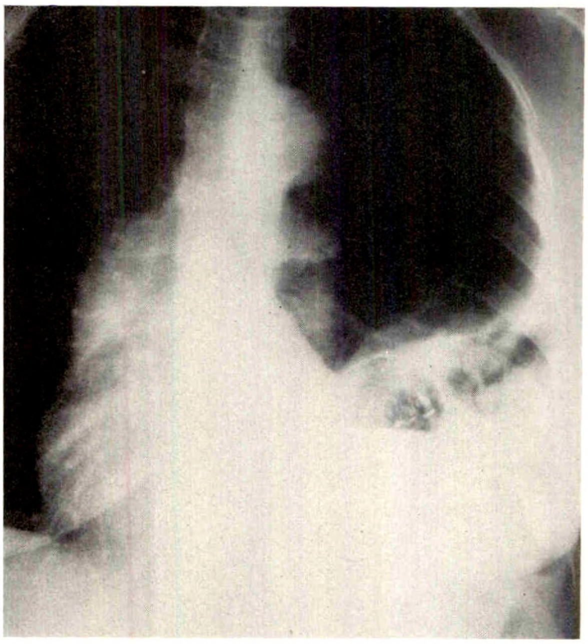


FIG. 3.

♂ Motor accident.
Chest X-ray shows apparent eventration of the diaphragm. Gastric herniation through a torn diaphragm was found at operation eight days later.



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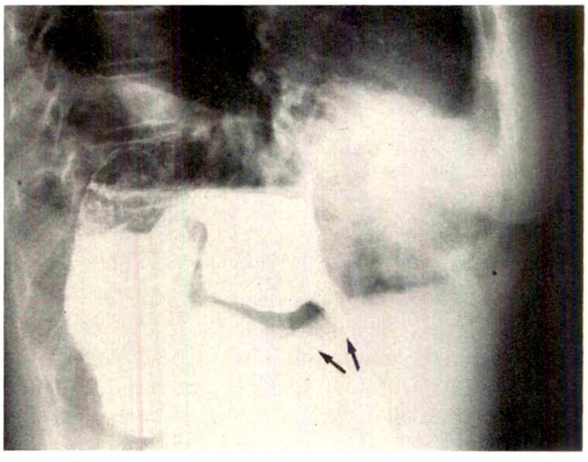


B

FIG. 4.

♀ R.T.A. six years previously.
(A) Erect film with bowel gas at the left base.
(B) Lateral film of barium meal showing herniated and rotated stomach (arrows) in the chest. Small and large bowel herniations were also found at operation.

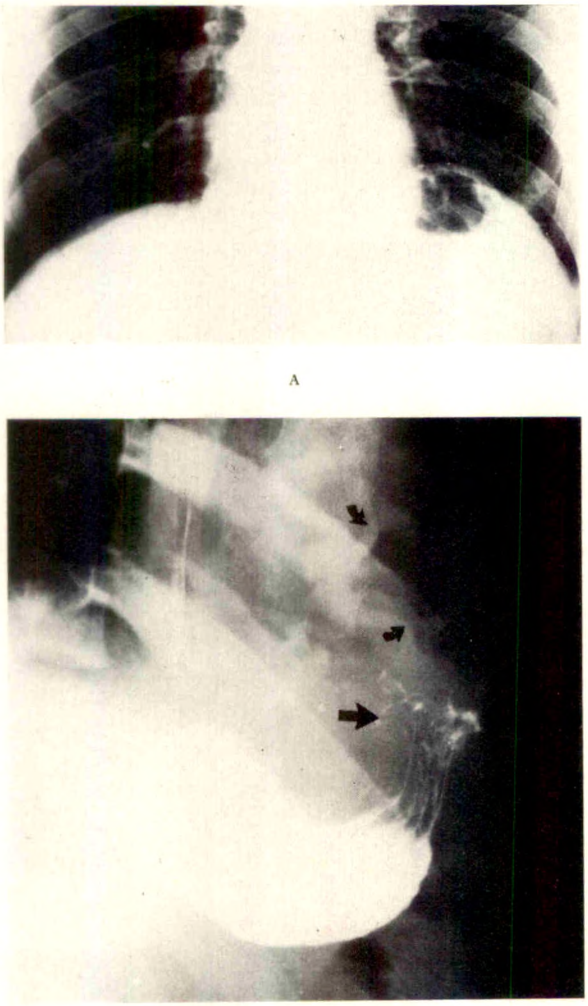


Fig. 5.

♂ L. chest postero-lateral stab wound ten weeks old. Previous chest X-ray showed a small left basal effusion. (A) Erect film with raised hemidiaphragm.

(B) Barium meal. The gastric body points upwards and is obstructed (straight arrow). Gas in the herniated stomach is also seen (curved arrows). Herniated small bowel was also found at operation.

and splinted diaphragm due to fractured ribs (Grage *et al.*, 1959). When the bowel is fluid-filled or the hernia is occupied by omentum, spleen or liver, the solid shadow at the base can be misinterpreted as pulmonary contusion, collapse, infection or infarction (Fig. 2: Mansour *et al.*, 1975).

Some patients wrongly diagnosed as having a pneumothorax or pleural effusion have had pleural drainage attempted, this can result in intrathoracic bowel perforation (Carter *et al.*, 1951; Lernau *et al.*, 1959). To avoid this serious iatrogenic complication and to exclude or establish the diagnosis of traumatic herniation, barium studies should be done.

The most typical and diagnostic appearance of a barium-filled loop of bowel herniated through the diaphragm is the approximation and narrowing of its afferent and efferent limbs as they pass through the tear (Fig. 4B). There are however variations on this basic theme. The afferent limb may be so narrowed as to prevent contrast medium getting into the herniated loop at all (Fig. 5B) or the efferent limb may be narrowed enough to prevent contrast medium going beyond the loop (Fig. 1B; Carter *et al.*, 1951; Grimes, 1974).

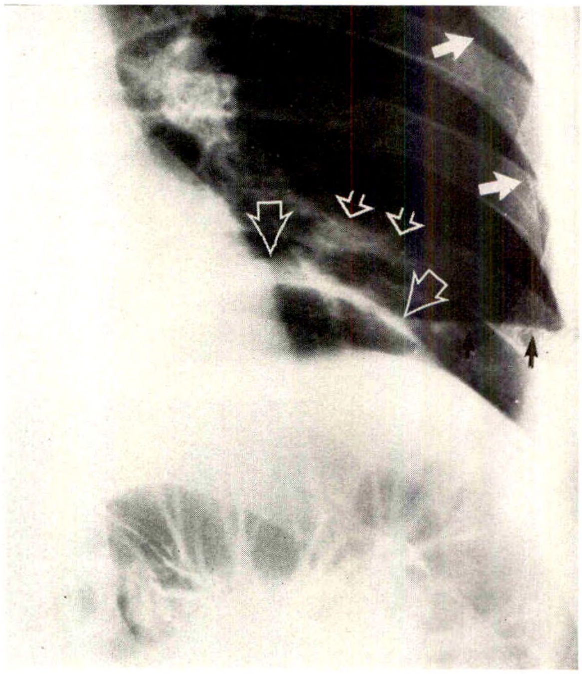
A special situation exists where the hernia consists purely of gastric fundus; this caused some of our longer diagnostic delays. This is because the gastric fundus is in effect a "blind alley"; contrast medium can pass freely through the oesophagus, body of stomach and duodenum without ever having to enter the fundus and thus one does not see any of the typical and readily visible signs of the herniated loop. It is, therefore, important to see the fundus filled with contrast medium; if it does not fill in spite of tilting the patient head down or if there is only a short projection pointing towards it, then this "amputated fundus" sign becomes specific for herniation (Figs. 6B, 7B). Alternatively the fundus may fill but with a constriction as it passes through the tear (Fig. 6D). If barium does not fill the fundus, air insufflated through a naso-gastric tube with the patient erect may do so (Fig. 7B). Rectal air insufflation can similarly be used when barium cannot be made to enter a colonic herniation.

An abdomino-pelvic crush injury may cause a tear too large to produce any of these diagnostic signs on barium study *i.e.* no approximation of limbs, no narrowing and no fundal amputation (two patients).

In none of our patients was herniation of the small bowel present without accompanying stomach or colon so it seems that contrast examinations of the stomach and colon are all that is necessary and that "follow-through" radiographs of small bowel are superfluous.

Tears without herniation

In the 22 patients in this category, plain radiographs were normal in eight, showed only mild elevation of the hemidiaphragm with a little blood in the costophrenic recess in eight and more obvious haemo- and/or pneumothorax in six. Thus even when there are abnormalities, these are of the type found in most cases of trauma to the rib cage or lung and would not lead one to suspect diaphragmatic



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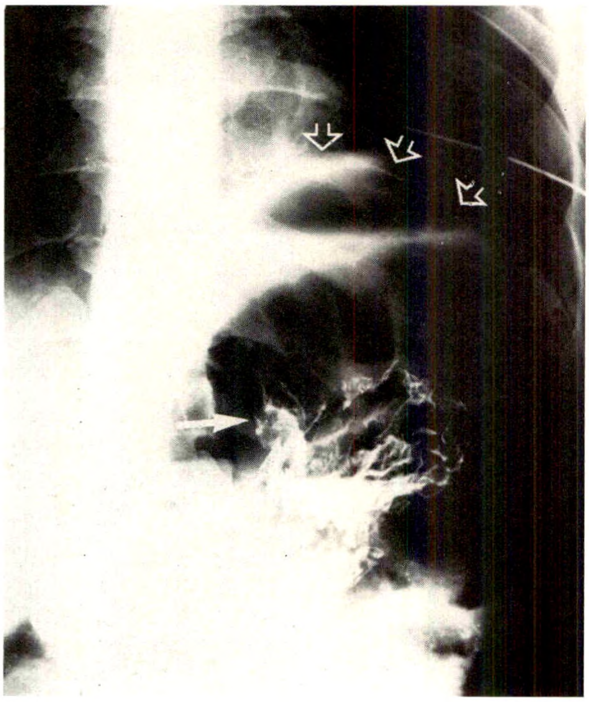

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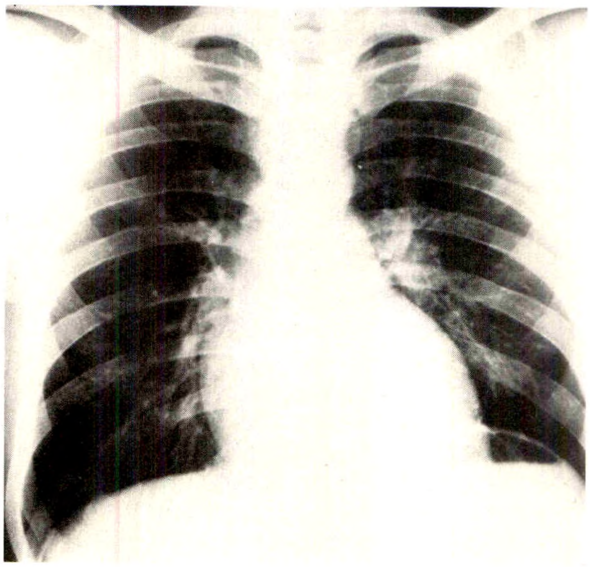

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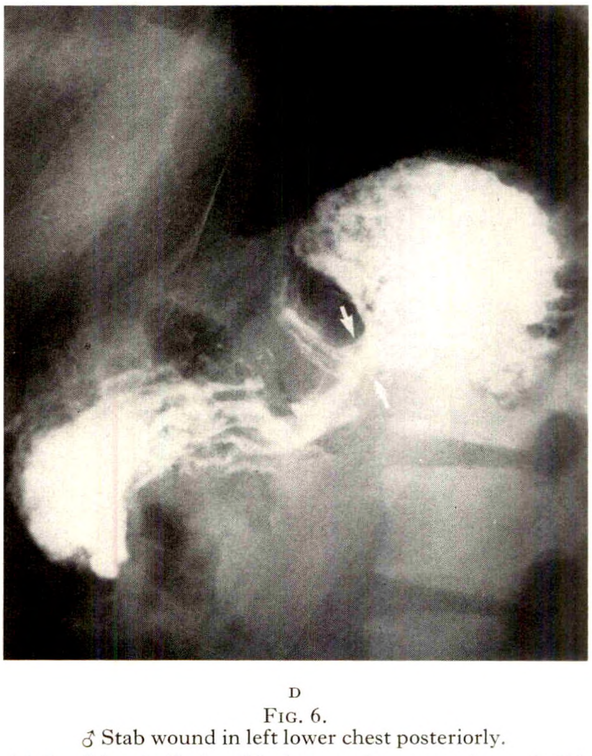


D

Fig. 6.

♂ Stab wound in left lower chest posteriorly.

(A) Small basal effusion (black arrows), pneumothorax (solid white arrows) and herniated gastric fundus (open arrows) are shown.

(B) Gas in a fundal hernia (open arrows) and gastrografin in the cardia (closed arrow) are seen. The significance was not recognized at that time.

(C) CXR 17 months later.

(D) Barium meal. Stenosis at point of herniation shown (arrows).

injury. Even if it were suspected, barium studies of stomach and colon would be normal in the absence of herniation.

However the diagnosis can sometimes be made on very basic clinicoradiological correlations. If a pneumothorax is found after a stab injury to the abdomen alone, then this automatically means the diaphragm has been breached. Similarly specific is the opposite situation where a downward stab into the chest produces a pneumoperitoneum or clinical features suggesting trauma to liver, spleen or bowel (two patients). Where only clinical suspicion is suggestive of a torn diaphragm, diagnosis may be made by the appearance of intrapleural gas following diagnostic pneumoperitoneum (McCort, 1966). Many of these patients have peritoneal lavage for the diagnosis of intra-abdominal injury (Worth, 1976) and the gas could be conveniently insufflated through the same peritoneal dialysis catheter, but this would not be possible if a pneumothorax was present and false-negative results may result from plugging of the tear by viscus or omentum.

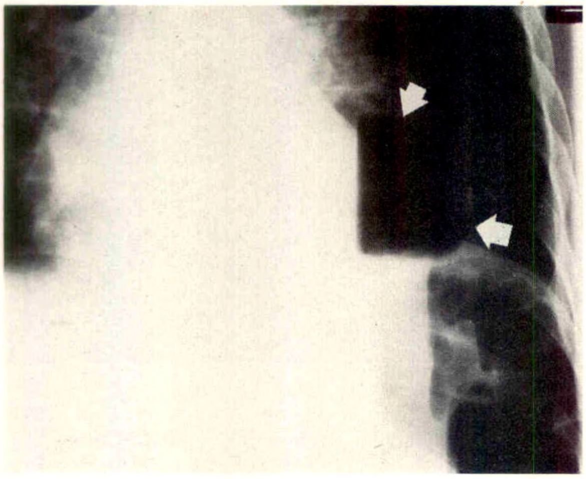
Other points

There is a marked left-sided preponderance in all series including our own and several factors can be considered.

1. The liver may protect the right hemidiaphragm from the sudden rise in pressure caused by abdomino-pelvic blunt trauma (Tan *et al.*, 1973; Gourin and Garzon, 1974; Wise *et al.*, 1973).

2. Even when the right hemidiaphragm is torn, the liver tends to be in the way so bowel herniation rarely occurs (not at all in our series); and as it is usually bowel herniation which is responsible for the symptoms arising from torn diaphragm, many right-sided tears may therefore not come to clinical attention.

3. One might in addition speculate that most victims are stabbed from in front by a right-handed assailant thus injuring the left hemidiaphragm; but



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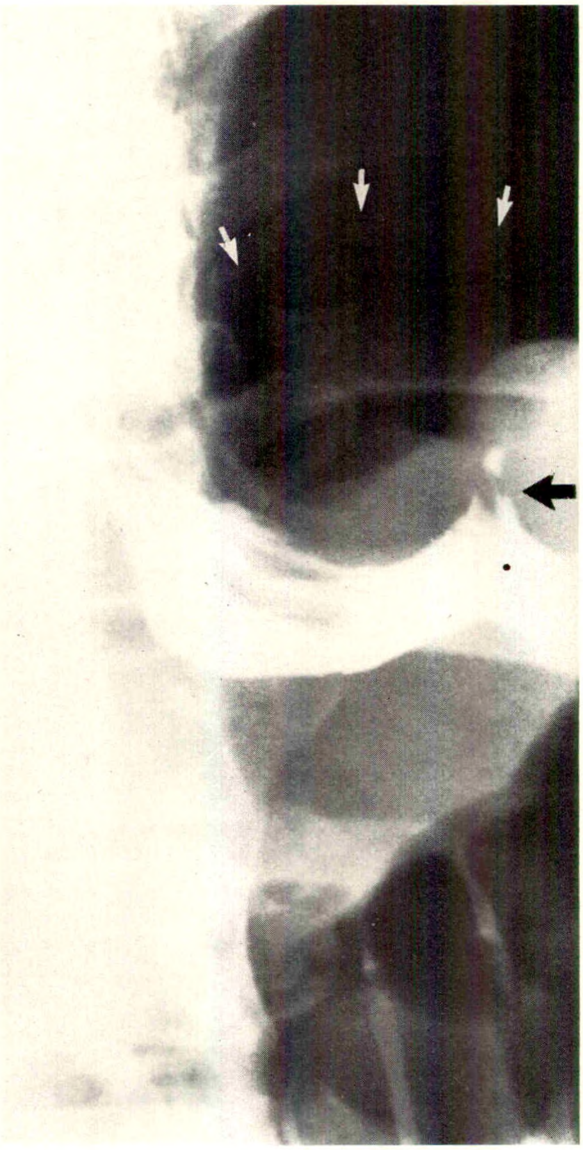

B

Fig. 7.

♂ Stab wound.

(A) A gas and fluid collection is shown in the left lower chest. (B) Barium meal. There is obstruction (black arrow) to the passage of barium into the herniated fundus (white arrows). "amputated fundus" sign.

in fact many of the stab wounds in our series were inflicted in the back so this argument does not hold.

The fact that five of our 11 cases due to motor vehicle accidents had an associated pelvic fracture is in keeping with the experience of Grage *et al.* (1959) that when a ruptured diaphragm is present after such an incident, a pelvic fracture is present in more than half the cases. Although the reverse association is less common, the chest radiograph should be examined for features suggestive of herniation whenever a pelvic fracture is diagnosed (Fig. 3).

REFERENCES

CARTER, B. H., GIUSEFFI, J., and FELSON, B., 1951. Traumatic diaphragmatic hernia. *American Journal of Roentgenology*, *65*, 56–72.
EFRON, G. and HYDE, I., 1967. Non-penetrating traumatic rupture of the diaphragm. *Clinical Radiology*, *18*, 394–398.
GOURIN, J., and GARZON, A. A., 1974. Diagnostic problems in traumatic diaphragmatic hernia. *Journal of Trauma*, *14*, 20–31.
GRAGE, T. B., MACLEAN, L. D., and CAMPBELL, G. S., 1959. Traumatic rupture of the diaphragm. *Surgery*, *46*, 669–681.
GRIMES, O. F., 1974. Traumatic injuries of the diaphragm. *American Journal of Surgery*, *128*, 175–181.
HILL, L. D., 1972. Injuries of the diaphragm following blunt trauma. *Surgical Clinics of North America*, *52*, 611–624.
LERNAU, O., BAR-MAOR, J. A., and NISSAN, S., 1974. Traumatic diaphragmatic hernia simulating acute tension pneumothorax. *Journal of Trauma*, *14*, 880–884.
MANSOUR, K. A., CLEMENTS, J. L., HATCHER, C. R., and WALTERS, D. A., 1975. Diaphragmatic hernia caused by trauma. *American Journal of Surgery*, *41*, *97–104*.
MCCORT, J. J., 1966. *Radiographic examination in blunt abdominal trauma*, pp. 159–175 (W. B. Saunders, Philadelphia).
TAN, G. C., HAMILTON, S. G. L., GIBSON, P., and SIMPSON, J. A., 1973. Ruptured diaphragm: experience in a major accident centre over a ten-year period. *Australian and New Zealand Journal of Surgery*, *43*, 163–168.
WORTH, M. H., 1976. Abdominal trauma. *Journal of the American Medical Association*, *235*, 853–854.

Book review

Advances in Oto-rhino-laryngology, Vol. 24, Modern Methods of Radiology in ORL. Volume editors: S. Brunner, and P. E. Andersen, pp. 196, illus., 1978 (S. Karger, AG., Switzerland), DM.133.

This volume contains selected papers from the 7th International Congress of radiology in oto-rhino-laryngology, held in Copenhagen during 1976. The Congress brought together a group of eminent people concerned with the advancement of knowledge in the field of radiology in ORL.

The collected papers of varying length and quality present some clinical aspects and applications of the newer radiological techniques as witnessed two years ago. The long latent period from presentation to publication in an environment of rapidly-changing technologies is unfortunate.

There are seven communications concerned with CT, one with thermography of the neck, one with scintigraphy of bone and the remainder on various applications of conventional tomography. The presentations cannot be considered a comprehensive appraisal of modern imaging methods but there are nevertheless important features to commend to the reader.

Tomographic evaluation of the vestibular aqueduct is considered by Wilbrand from Uppsala in the assessment of Meniere's disease and by Valvassori and Clemis in the consideration of cochleo-vestibular disorders. The anatomical studies of Wilbrand and the practical clinical approach of both papers make valuable contributions to the literature on this controversial subject. Phelps and Lloyd describe a specific inner ear deformity characterized by tapering of the IAM and dilatation and dysplasia of the labyrinth. This deformity, which carries an increased risk of CSF leak, appears to be a distinct entity different from the Mundini deformity.

The group of papers concerned with the clinical application of CT albeit at that time based on limited experience, accurately forecast the present role of the technique in ORL.

The book is well produced with high-quality illustrations but it must be apparent to the publishers and the reader that conference proceedings are most useful when produced at or immediately after a meeting. It seems less than fair to the expert authorship that new ideas and presentations should be left stranded on a publication sandbank by the rapidly changing tide of technological development. Modern printing methods permit top-quality illustrations to be produced rapidly and cheaply, particularly in paperback form. This 196-page hardback costs more than £30.

IAN ISHERWOOD.

1979, *British Journal of Radiology*, 52, 382–387

Fissuring of the posterior annulus fibrosus in the lumbar spine

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ABSTRACT

Severe back-ache in young adults may present a difficult clinical problem when the absence of neurological signs results in delayed diagnosis. Fourteen patients, with discographic evidence of posterior annular fissuring are reported. The discrepancy between painful disability and negative radiographic examination including radiculography is stressed. Discography has proved to be the investigation of choice in these patients. This will demonstrate the morphology of the lesion and reproduce the symptomatology in the majority of cases. The clinical implications are discussed.

Classification of back-ache is difficult and a precise diagnosis cannot be given in the majority of sufferers. The purpose of this study is to describe a group of patients under the age of 40 with the predominant symptoms of disabling back-ache in the presence of characteristic radiological findings. The absence of clinical signs, particularly of nerve entrapment, resulted in long delay in the recognition of subtle evidence of disc damage. However, increased clinical awareness has subsequently made possible earlier detection of such lesions.

CLINICAL MATERIAL

Four hundred patients who have undergone comprehensive radiological investigation in the X-ray Department of the Robert Jones & Agnes Hunt Orthopaedic Hospital for severe disabling low back pain have been reviewed. From this large series, 14 cases have been found with evidence of a fissure in the posterior annulus fibrosus demonstrated by discography. The standard radiographic examination of the lumbar spine was normal in each instance and the discogram was necessitated by severe disabling back-ache.

CLINICAL FINDINGS

Of the 14 patients, there were equal numbers of males and females. Their ages ranged from 16 to 40, the average being 26.3 years. The circumstances of onset were recorded as follows: sport (4), industry (3), fall (2), direct blow to the back (2) and spontaneous (3).

The distribution of pain was recorded on homunculus diagrams. All 14 patients had central low back pain extending into the buttocks. In seven, unilateral leg pain extended down the back of the thigh to the knee and in another four the pain reached down to the ankle. The duration of symptoms ranged from three months to seven years and the average was three years and nine months. The level of disability was graded as follows:

Grade 1; no disability (no patients).

Grade 2; mild disability, altered lifestyle but no loss of income (one patient).

Grade 3; moderately severe disability, significant loss of normal, social and work activity resulting in considerable loss of income (eight patients).

Grade 4; severe disability resulting in unemployment, loss of status and change in lifestyle (five patients).

Clinical examination was notable for the absence of specific findings. There was restriction of spinal movement in three patients and two had straight leg raising limitation in the 40/70 deg. range. It should be emphasized that the remainder had no detectable physical signs.

RADIOLOGICAL INVESTIGATION

Preliminary standard radiographs of the lumbar spine showed no evidence of vertebral anomaly, disc degeneration, spondylosis or instability in any of the patients. Initially seven patients were subjected to metrizamide radiculography augmented in some instances by epidural venography. These examinations showed no evidence of nerve root entrapment although mild central disc bulging was occasionally present. In the later patients of the series radiculography was not felt to be justified and discography became the initial investigation of choice. Discography was performed using the lateral oblique approach for L.3/4 and L.4/5 and a transdural puncture for the lumbo-sacral disc space. Care was taken to ensure adequate filling of the nucleus with contrast medium so that minor degrees of extravasation through annular fissuring could be recognized consistently. A small tear may be evident only after

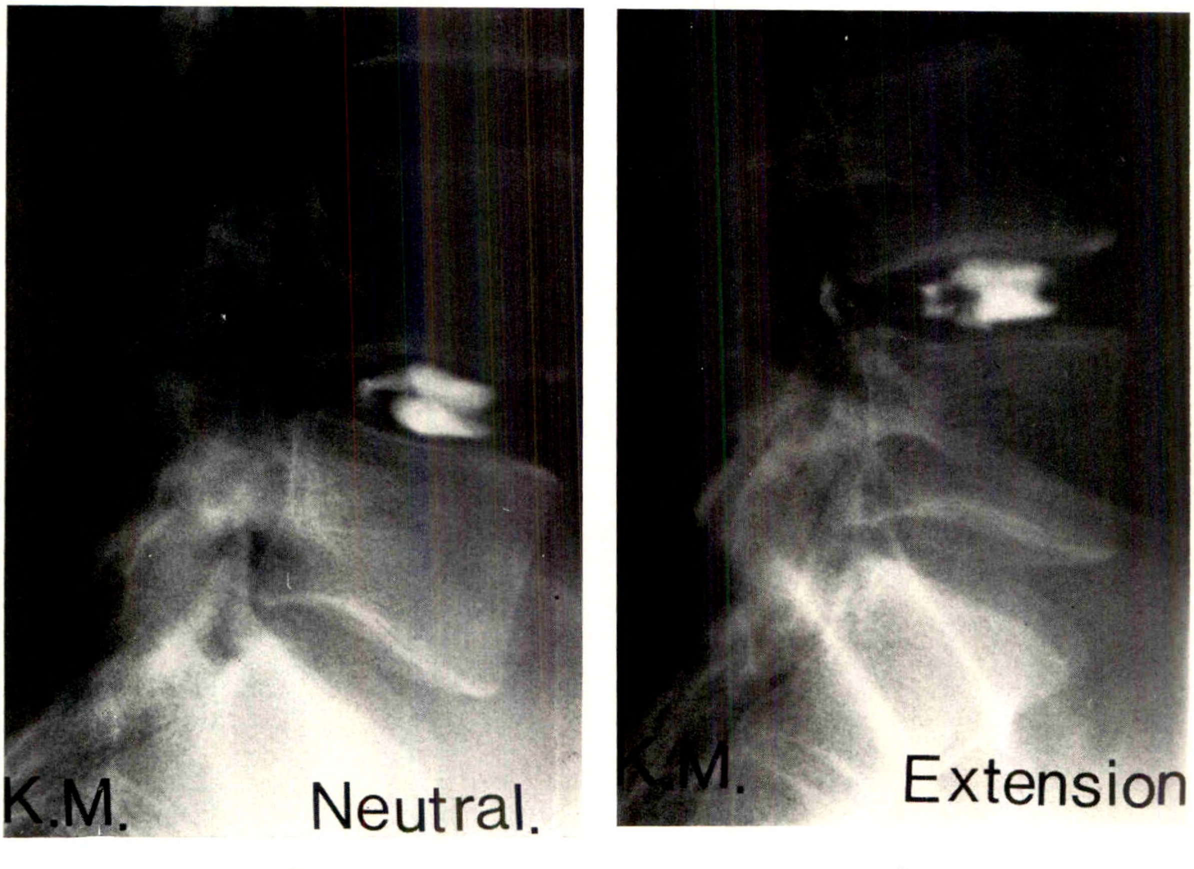

FIG. 1.

L.4/5 discogram.

(A) Neutral position. The contrast is contained within the nucleus.

(B) Extension position. Following forward and backward bending manoeuvres a small "collar stud" extravasation of contrast is seen posteriorly, indicating a radial tear through the posterior annulus and the nucleus.

dynamic bending, or delayed films are taken (Fig. 1). Good radiographic technique with careful collimation of the X-ray beam is essential. The abormality in the annulus is identified by a "collar stud" type of extravasation which extends backwards from an otherwise normally outlined nucleus.

Discography revealed normal nuclei in all patients at the L.3/4 level. At L.4/5, 12 out of the 14 nucleograms were normal and two showed evidence of rupture. At the lumbo-sacral junction there was one normal disc and 13 annular ruptures. Injection of contrast into the abnormal disc complex reproduced part or all of the symptomatic pain pattern in 12 patients. Figure 2 shows a comparison between the symptomatic pain pattern (described by the patient on admission, and illustrated on the clinical photograph) and the distribution of pain referral provoked by the discogram. These induced patterns were drawn by an independent observer without prior knowledge of the other record. In the example illustrated, the symptomatic pain pattern extends across the low back and buttocks and down the outside of both legs. There is an associated cruciate distribution of interscapular pain. The provocation pain pattern extended across the low back and only down the right leg. The correlation between symptomatic and discographically induced pain is illustrated in Fig. 3.

It was noted that two patients did not have pain reproduction by discography. On review it was evident that both had a different radiographic appearance. The contrast medium clearly extravasated into the epidural space and was not contained within the confines of the posterior annulus fibrosus (Fig. 4). Injection of local anaesthetic into the symptomatic and abnormal nucleus abolished the induced pain pattern in five patients. There were no complications of discography.

OPERATIVE FINDINGS

Eleven patients have undergone surgery because of severe pain or significant disability. At operation, no evidence of a disc prolapse was found, but in each case a large rent was demonstrated, penetrating through all layers of the annulus fibrosus which correlated with the discogram (Fig. 5). The clinical response to surgery will take some time to evaluate, and the results will form the basis of a separate communication.

DISCUSSION

The most striking clinical feature in the patients of this small series, was the severe disabling pain and its profound limitations on subsequent lifestyle in social, economic and psychological terms. The

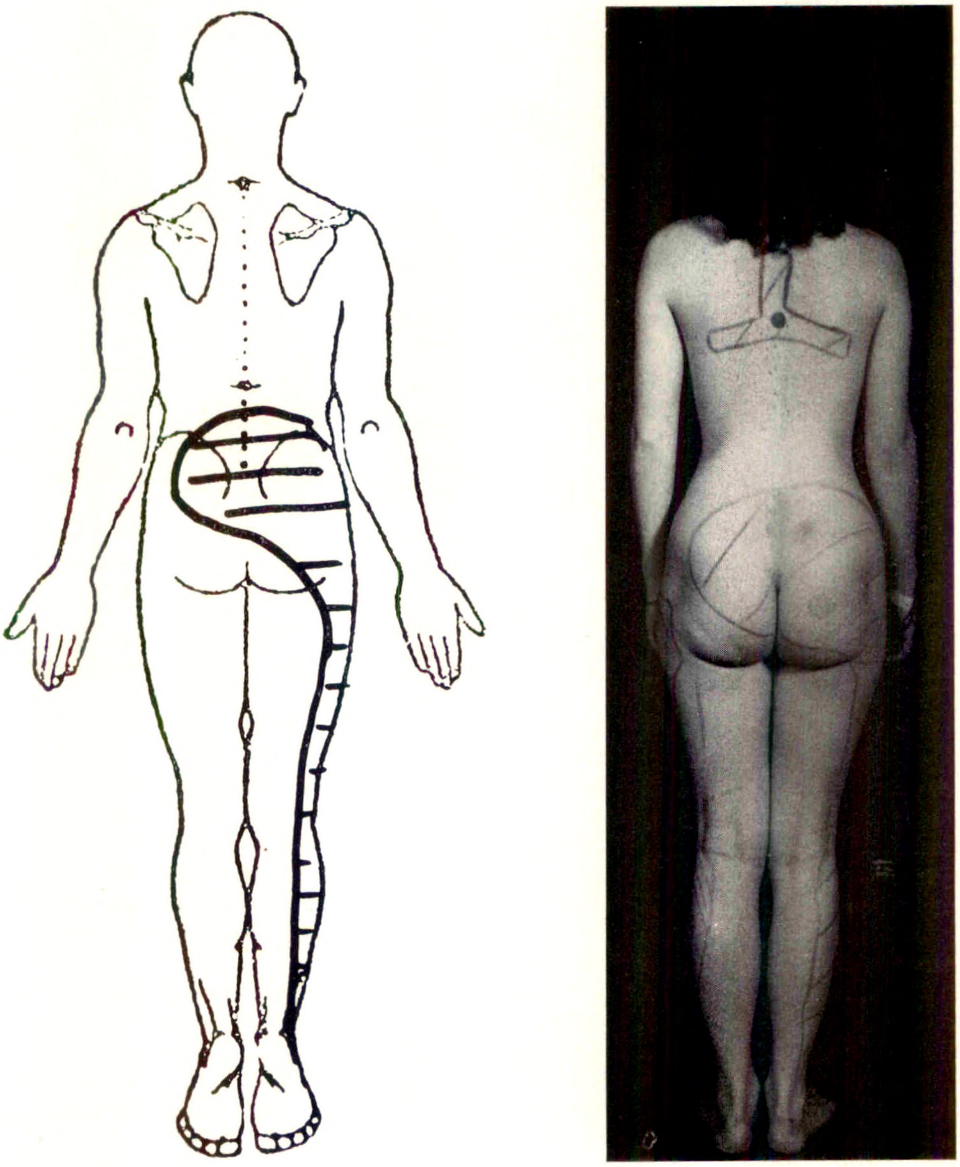

FIG. 2.

Pain patterns. The homunculus diagram on the left illustrates the distribution of pain induced by the discogram. The clinical photograph shows the symptomatic pain pattern described by the patient on admission. The records were made by independent observers.

absence of specific neurological findings suggesting nerve root entrapment or compression makes it understandable that clinicians are unlikely to feel that invasive studies such as radiculography or discography will be helpful. In this respect annular fissuring may resemble disc herniation in the adolescent, where it has been observed that diagnostic confusion is usually due to failure of the physician to recognize the entity as a cause of back or sciatic pain (Bradford and Garcia, 1971).

Structural changes in the lumbar annulus fibrosus have been widely studied (Schajowicz, 1953; Hirsch *et al.*, 1963; Schmorl and Junghanns, 1971; Parke and Schiff, 1971; Vernon-Roberts, 1976). It is well known that clefts and fissures in the annulus are notorious artefacts produced by the preparation of

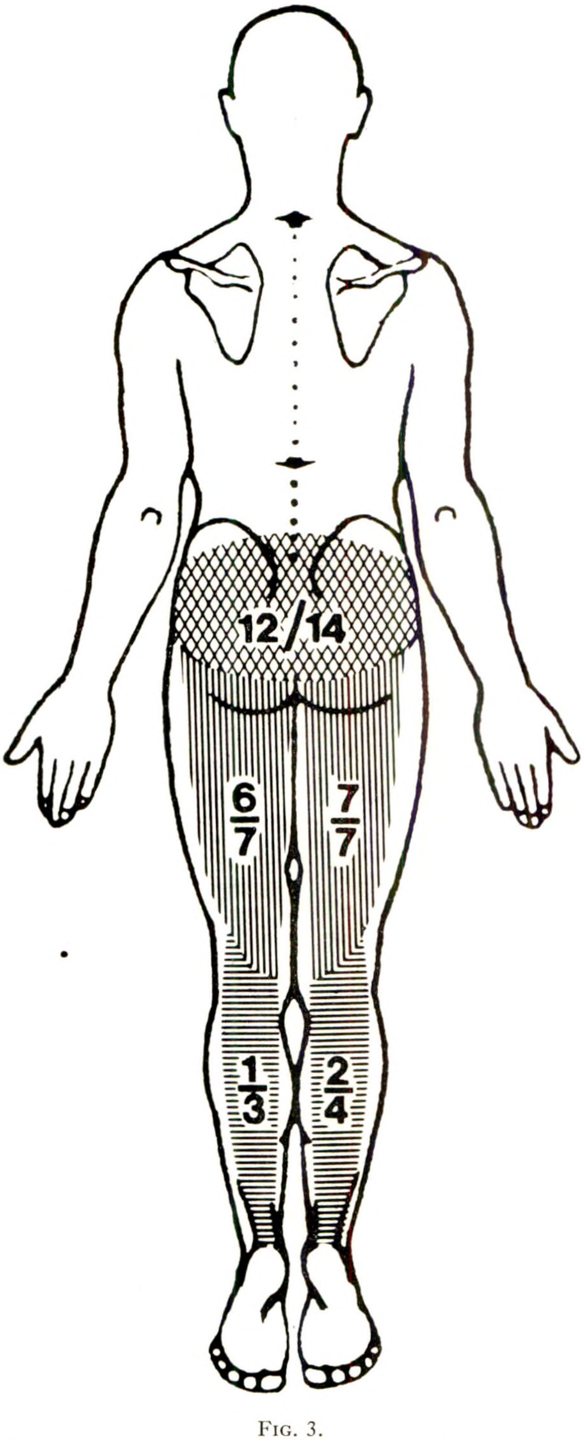

FIG. 3.
Correlation between symptomatic and discographic pain. Symptom reproduction occurred in the low back in 12 out of 14 patients. In the left thigh in six out of seven and in the left lower leg in one out of three. The distribution in the right leg was seven out of seven in the thigh, and two out of four in the lower leg.

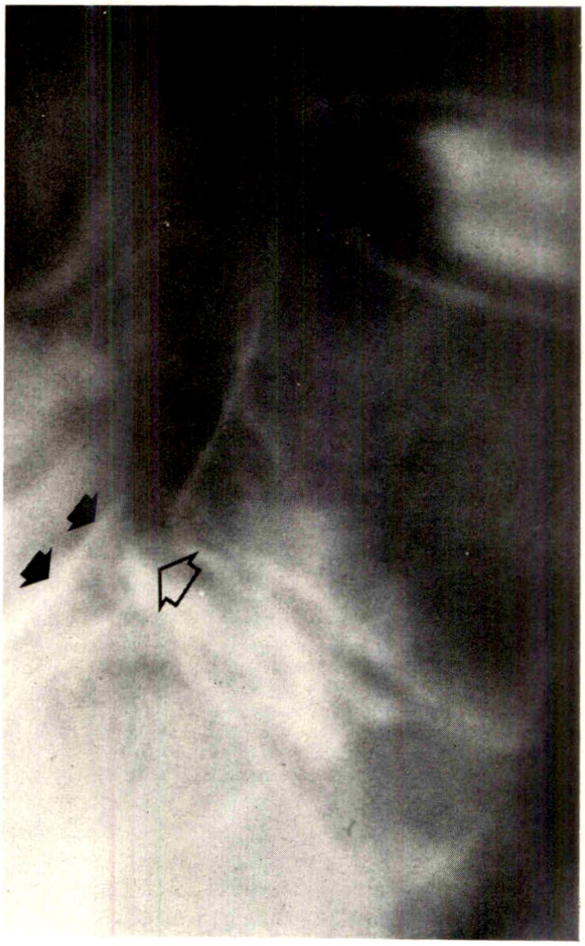

FIG. 4.
Complete annulus rupture—lumbosacral discogram. Contrast medium extravasates from the nucleus into the epidural space (closed arrows) through a large posterior annular defect (open arrow).

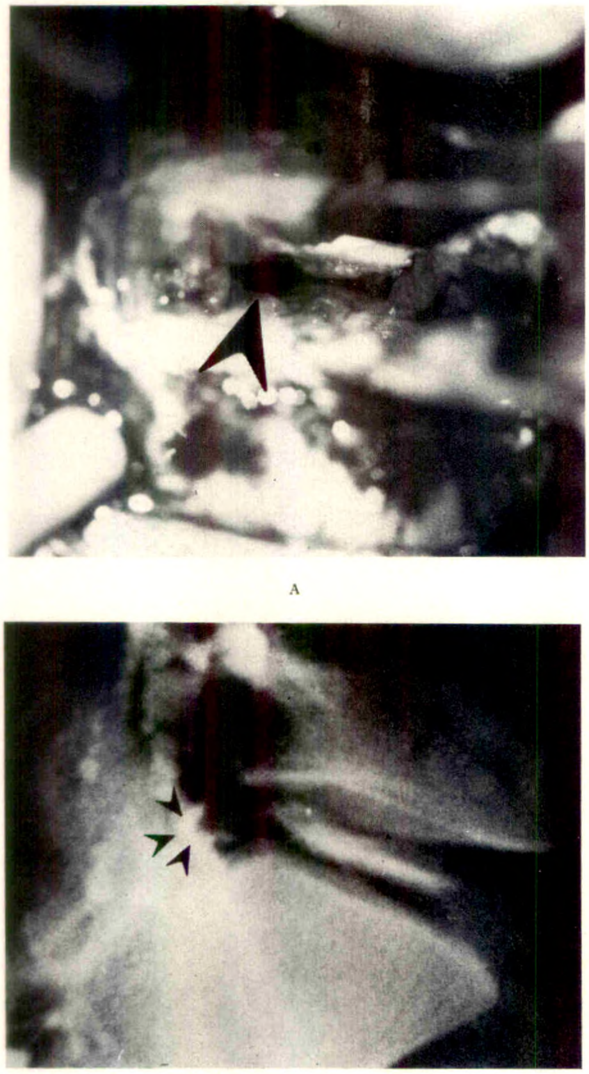

FIG. 5.

Operative correlation with discogram. (A) Surgical findings. The intervertebral disc lies transversely across the operating field. The radial cleft extends through all layers of the annulus fibrosus (arrow).

(B) Pre-operative discogram. Contrast extravasates radially in characteristic collar-stud configuration (arrows). Thecal residues of a previous myelogram are still present.

histological material. However, true tears occur with considerable frequency in elderly subjects, often accompanied by invading fibro-vascular tissue which provides evidence of antecedent disruption and repair. Clefts may be present in young adults occasionally involving the annulus alone and usually arranged in concentric fashion. This can lead to separation of portions of disc tissue or even complete rupture into the epidural space.

The frequency of findings on pathological examination clearly indicates that not all lesions can be symptomatic and there has been much speculation about the source of pain (Roofe, 1940; Inman and Saunders, 1947; Lindahl and Rexed, 1951; Morgan and King, 1957; Cloward 1963; Ramani *et al.*, 1975; Crock 1976, Nachemson, 1976).

It is difficult to assess the sensitivity and specificity of lumbar discography because the examination is invasive and cannot be justified in asymptomatic volunteers. Review of 180 discograms performed on back-ache patients under the age of 40 show that 107 had been performed at L.3/4, 148 at L.4/5 and 100 at the lumbo-sacral level. The findings followed the expected distribution for each disc space. Normal discs were demonstrated in 82% of injections at L.3/4, 52% at L.4/5 and 27% at L.5/S1. At the lumbo-sacral disc, degeneration was present in 58 and disc narrowing with annular fissuring occurred in 12. Only 14 out of the total had defects in the annulus fibrosus as an isolated finding. Therefore this lesion is rare in the absence of other radiological signs of disc damage or degeneration. It is possible that this defect represents an early stage of disc injury. If so, then the lumbo-sacral disc would appear to be particularly vulnerable in the younger age group since autopsy examination of older patients shows a fairly uniform distribution of lesions at the lower three lumbar levels (Ball, 1978). Cadaveric discography has been performed on ten specimens from patients under the age of 40 who died of causes unrelated to back-ache. A total of 49 discs were injected, 37 were normal and 10 were degenerate. Two examples were found of posterior annular rupture from an otherwise intact nucleus. In addition, complete radial rupture of the posterior annulus has been found in an 18 year old patient who died of head injuries as a result of a motor-cycle accident. It was assumed that the disc injury resulted from the same traumatic episode.

There is strong clinical evidence that a variety of disc lesions associated with different syndromes may follow either single or repeated exposure of the spine to stress (Hult, 1954; Beals and Hickman, 1972). Eleven out of our 14 patients were able to relate the onset of their symptoms to a clearly remembered traumatic episode. It has been suggested by Farfan *et al.*, (1970) that malalignment of apophyseal joints produces torsional stress on the intervertebral segment which predisposes to disc damage in vulnerable patients. This did not appear to be a primary factor in the group of patients under study. Perhaps it might be suggested that fissuring of the annulus fibrosus represents early evidence of disc injury. Depending on the degree of damage, irreversible change may occur in this vulnerable region which culminates either in frank disc protrusion or disc degeneration. In an experimental study of intervertebral disc bursting pressures, Jayson *et al.*, (1973) found significant differences depending on nuclear morphology. Much lower pressures were required to burst postero-lateral hernia, central posterior hernia and degenerate nuclei, in postero-lateral and posterior directions.

Symptom reproduction by discography is well documented (Key, 1945; Wiberg, 1949; Fernström, 1960). Twelve out of the 14 patients had at least one component of pain provoked by the procedure. It is of interest to note that the two patients with asymptomatic discograms, demonstrated complete radial rupture of the annulus with epidural extravasation. It is possible that pain provocation with an intact nucleus, must somehow be the result of a transference of increased nuclear tension to the annulus region which does not occur in the presence of radial fissuring. Intra-nuclear injection of local anaesthetic blocked the induced pain symptoms in five patients and this suggests that the annulus can be a potential pain trigger point (Steindler, 1947). Clinically these lesions did not respond to conservative treatment and therefore do not represent the usual type of acute back syndrome where 90% of episodes respond to simple, symptomatic therapy (Dillane *et al.*, 1966). This disparity between severe symptomatology and paucity of clinical signs has been reported in other conditions. Crock (1976) has used the term "internal disc disruption" to describe a pattern of symptoms which is sometimes associated with constitutional upset, suggesting an auto-immune hypersensitivity reaction. Morgan and King (1957) have reported a syndrome with pain and few clinical signs, in the presence of lumbar intervertebral instability which is usually evident at the L.4/5 level.

In conclusion the diagnosis of fissuring of the posterior annulus fibrosus, should be considered in adolescents or young adults who are severely disabled with back-ache, in the absence of clinical or neurological findings and apparently normal standard X-rays. The offending lesion can be identified by discography and confirmed at surgery in selected instances. Early evidence suggests that, when conservative treatment fails, surgery can favourably influence the outcome.

REFERENCES

Ball, J., 1978. Personal communication.

Beals, R. K. and Hickman, N. W., 1972. Industrial injuries of the back and extremities. *Journal of Bone and Joint Surgery*, *54*, 1593–1611.

Bradford, D. S. and Garcia, A., 1971. Lumbar intervertebral disc herniations in children and adolescents. *Orthopaedic Clinics of North America*, *2*, 583–592.

Cloward, R. B., 1963. Lesions of the intervertebral discs and their treatment by interbody fusion methods. The painful disc. *Clinical Orthopaedics*, *27*, 51–77.

Crock, H. V., 1976 Traumatic disc injury. From the *Handbook of Clinical Neurology* by P. J. Vinken and G. W. Bruyn. Injuries of the spine and spinal cord, Part I, Chapter 19, 481–511.

Dillane, J. B., Fry, J. and Kalton, G. 1966. Acute back syndrome—a study from general practice. *British Medical Journal*, *2*, 82–84.

Farfan, H. F., Cossette, J. W., Robertson, G. H., Wells, R. V. and Kraus, H. 1970. Effects of torsion on the lumbar intervertebral joints. *Journal of Bone and Joint Surgery*, *52A*, 468–497.

Fernström, U., 1960. A discographical study of ruptured lumbar intervertebral discs. *Acta Chirurgica Scandinavica Supplementum*, 2–58.

Hirsch, C., Ingelmark, B. E. and Miller, M., 1963. The anatomical basis for low back pain. *Acta Orthopaedica, Scandinavica*, *33*, 1–17.

Hult, L., 1954. The munk fors investigation. *Acta Orthopaedica, Scandinavica, Supplementum 16*, 1–76.

Inman, V. T. and Saunders, J. B. De C. M., 1947, Anatomicophysiological aspects of injuries to the intervertebral disc. *Journal of Bone and Joint Surgery*, *29*, 461–475.

Jayson, M. I. V., Herbert, C. M., and Barks, J. S., 1973. Intervertebral discs: nuclear morphology and bursting pressures. *Annals of Rheumatic Diseases*, *32*, 308–315.

Key, J. A., 1945. Intervertebral disc lesions are most common cause of low back pain with or without sciatica. *Annals of Surgery*, *121*, 534–544.

Lindahl, O., and Rexed, B. 1951. Histologic changes in spinal nerve roots of operated cases of sciatica. *Acta Orthopaedica Scandinavica*, *20*, 215–225.

Morgan, F. P., and King, T., 1957. Primary instability of lumbar vertebrae as a common cause of low back pain. *Journal of Bone and Joint Surgery*, *39B*, 6–22.

Nachemson, A. L., 1976. The lumbar spine—an orthopaedic challenge. *Spine*, *1*, 59–71.

Parke, W. W. and Schiff, D. C. M., 1971. The applied anatomy of the intervertebral disc. *Orthopaedic Clinics of North America*, *2*, 309–324.

Ramani, P. S., Perry, R. H. and Tomlinson, B. E., 1975. Role of ligamentum flavum in the symptomatology of prolapsed lumbar intervertebral discs. *Journal of Neurology and Neurosurgery Psychiatry*, *38*, 550-557.

Roofe, P. G., 1940. Innervation of annulus fibrosus and posterior longitudinal ligament. From the Department of Anatomy, University of Louisville School of Medicine (unpublished).

Schajowicz, F., 1953. Studies on structural changes in the lumbar annulus fibrosus. *Acta Orthopaedica Scandinavica*, *22*, 184–231.

Schmorl, G., and Junghanns, R., 1971. *The Human Spine in Health and Disease* (Grune and Stratton, New York and London).

Steindler, A., 1947. An analysis and differentiation of low back pain in relation to the disc factor. The newer pathological and physiological concepts of anterior poliomyelitis and their clinical interpretation. *Journal of Bone and Joint Surgery*, *29*, 455–460.

Vernon-Roberts, B., 1976. Pathology of degenerative spondylosis. Chapter 4. in *The Lumbar Spine and Back Pain.* Edited by M. I. V. Jayson (Sector Publishing Ltd. London).

Wiberg, G., 1949. Back pain in relation to the nerve of intervertebral disc. *Acta Chirurgica Scandinavica, Supplementum 19*, 211–221.

1979, *British Journal of Radiology*, *52*, 388–389

An alternative method of bowel preparation for barium enemas

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ABSTRACT

A double blind trial is described comparing two methods of bowel preparation prior to barium enema. In 40 randomly selected patients a significant improvement was obtained by the use of an intestinal perfusion method.

The degree of bowel cleanliness prior to double contrast barium examination is of paramount importance in the production of high quality radiographs. The diagnostic accuracy of such examinations depends on the absence of faecal residue which may lead to an erroneous diagnosis of tumour or polyp. The amount of time and expense expended on the pursuit of such bowel cleanliness, together with the multitude of methods and materials available only serves to illustrate that no one method is yet perfect.

Recent work (Hewitt *et al.*, 1973; Crapp *et al.*, 1975; Levy *et al.*, 1976; Wood *et al.*, 1976) has suggested that antegrade intestinal perfusion using iso-osmotic balanced electrolyte fluid is effective in emptying the bowel of faecal material. One of these groups recorded that this method of preparation left the bowel in a "pristine state" for colonoscopy. Other studies (Skucas *et al.*, 1976) involving the use of this method in fit young volunteers have also suggested a practical advantage over other methods.

METHOD

The study was conducted on outpatients of Westminster Hospital who were randomly selected by number after referral to the X-ray department for barium enema examination. The trial was carried out with the approval of the Ethics Committee of Westminster Hospital and the informed consent of the patients concerned. Those patients with a history of cardiac failure, impaired renal function or with clinical evidence of severe inflammatory disease or obstructing lesions of the bowel were excluded as were those patients who did not wish to take part.

A total of 41 patients entered the trial and were randomly divided by number into a treatment and a control group. The patients in the control group were prepared by castor oil (dose 25 ml) purgation 24 hours prior to the barium enema followed by colonic lavage on the morning of the examination. No complications of this method were recorded.

For the patients in the treatment group a 12 gauge naso-gastric tube was passed and confirmation of the correct site was obtained by aspiration of gastric contents. Hartmann's solution (Travenol) at 37°C was infused into the stomach at a rate of four litres per hour. Bowel evacuation and profuse diarrhoea followed after intervals ranging from 20 minutes to two hours. The infusions were discontinued when the diarrhoea fluid became clear. Time intervals for this to occur varied from one to two hours. The patients then waited for at least one further hour after which they were submitted to routine double contrast barium enema examination. The method of performing the examination and the films obtained were similar in all cases. Five films were available for assessment in each case; these being over table prone, supine, prone oblique and two decubiti. The radiographs were retrospectively submitted to a radiologist who was not concerned with the first part of the trial and was not informed of the particular method of preparation in each case. Each examination was assessed for degree of bowel cleanliness and diagnostic quality. Each was graded according to the following classification:

Grade 1—no visible faecal material present;
Grade 2—minimal faecal material present. Examination still of diagnostic quality;
Grade 3—heavy faecal contamination present such as to render the examination of poor diagnostic quality.

RESULTS

Statistical examination of these results (Table I) shows a significant difference in the quality of preparation between the two groups. Analysis by the chi squared test yields a value of chi squared of 9.32 (p less than 0.04 with two degrees of freedom).

TABLE I

	Treatment group			Control group		
Grade	1	2	3	1	2	3
Total patients	12	5	3	3	10	8

DISCUSSION

Most of the patients prepared by the infusion method did not experience undue discomfort although all showed clinical evidence of abdominal distension. None suffered respiratory embarrassment and chest radiographs taken on six of the patients showed only elevation of the diaphragm. The infusion did not produce abdominal colic and no increased incidence of spasm of the bowel was recorded. Four patients out of 20 did, however, vomit during the infusion and it is of interest to note that three of these patients were subsequently found to have colonic carcinomas. It appears probable that adjustment of infusion flow rate according to symptoms would avoid this problem. In one of these four the vomited material was noted to be slightly blood stained and as this occurred before the infusion was completed the patient was withdrawn from the trial and admitted overnight for observation. No further symptoms or signs developed in this patient. Despite random selection the three colonic tumours were all found in the infusion group, one being in the patient withdrawn from the trial and the remaining two, who completed the infusion, make up two out of the three patients whose examination showed gross faecal contamination. This is in marked contrast to the control group where eight examinations were allocated to grade three and only one had serious pathology. The only observed undesirable effect of intestinal perfusion on the quality of the examination was a significant degree of contrast medium dilution produced by retained Hartmann's solution in terminal small bowel and proximal colon. This occurred in only a few patients and in no case was it sufficient to make the examination non-diagnostic. It is anticipated that some reduction in this effect might be obtained by increasing the time interval between termination of the infusion and commencing the barium enema examination.

CONCLUSION

In a small series of patients intestinal perfusion with Hartmann's solution has been shown to be a safe and acceptable alternative method of preparation prior to barium enema which is capable of obtaining a significant improvement in the degree of bowel cleanliness. While we do not advocate that this method be adopted routinely as it is costly in terms of medical and nursing time, it may well be indicated in cases where colonic polyps and intraluminal tumours are suspected. It would also appear to be of value in the preparation of those patients in whom routine cleansing methods have proved inadequate and in patients in whom abdominal angiography is requested shortly after barium examination.

ACKNOWLEDGMENTS

We wish to thank Dr. T. D. Preston for his assistance in the statistical analysis and Dr. F. Starer for his help in the preparation of the paper.

REFERENCES

CRAPP, A. R., POWIS, S. J. A., TILLOTSON, P., COOKE, W. T., and ALEXANDER-WILLIAMS, J., 1975. Preparation of the bowel by whole gut irrigation. *Lancet*, *2*, 1239–1240.

HEWITT, J., RIGBY, J., REEVE, J., and COX, A. G., 1973. Whole gut irrigation in preparation for large bowel surgery. *Lancet*, *2*, 337–340.

LEVY, A. G., BENSON, J. W., HEWLETT, E. L., HERDT, J. R., DOPPMAN, J. L., and GORDON, R. S., 1976. Saline lavage: a rapid, effective and acceptable method for cleansing the gastro-intestinal tract. *Gastroenterology*, *70*, 157–161.

SKUCAS, J., CUTLIFF, W., and FISCHER, H. W., 1976. Whole gut irrigation as a means of cleaning the colon. *Radiology*, *121*, 303–305.

WOOD, P., HATFIELD, A., GREEN, J., and HAMILTON, S. M., 1976. Whole gut perfusion for therapeutic purgation. *British Medical Journal*, *1*, 433–434.

Book review

Experimental Radiological Health Physics. By D. A. Gollnick, pp. x+257, 1978 (Pergamon Press, New York) $9.75 soft cover $20.00 hardback.
ISBN 0–08–023201–9/0–08–020524–0 (paperback)

This is a manual describing 37 practical exercises to cover the experimental course for the American Certifications in Health and Radiological Physics. Each experimental procedure is prefaced with a synopsis of the underlying theory and the book is bound with spaces for data and calculations. The manual covers a wide field from basic radiation experiments through to radiation surveys, environmental monitoring and measurement of microwaves and laser beams. The full range of experiments requires a selection of apparatus that would only be available in the largest radiological laboratories.

Departments running M.Sc. courses might gain some ideas from the book but students would find the text confusing since it is written without reference to the gray, seivert or the recommendations of ICRU 26. There is a lack of detailed explanation for some of the experimental procedures *e.g.* foil activation. The book has some useful tables and graphs of radiological data both in the text and appendices but strangely no references are given to help students unravel the problems arising from the experiments.

N. F. KEMBER.

1979, *British Journal of Radiology*, *52*, 390–392

Ultrasound diagnosis and treatment of gall-bladder fossa collections following biliary tract surgery

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ABSTRACT

Three patients are presented with sterile or septic subhepatic fluid collections after biliary tract surgery. In each patient, the common clinical presentation was fever and ultrasound was primarily responsible for demonstrating its source. In one patient, percutaneous aspiration of the abscess under ultrasonic guidance obviated the need for any further treatment. We conclude that ultrasound is an effective method for investigating suspected fluid collections after biliary tract surgery. Aspiration of the lesion under ultrasonic guidance is a safe means for confirmation of the diagnosis and may be therapeutic as well.

Wound infection is a rather common complication of biliary surgery. Two recent studies have shown a 10.5 and 36% incidence of wound infections, most of which are subcutaneous (Keighley *et al.*, 1974). The most significant factors were whether the cholecystitis was acute or chronic, whether the bile was infected, and whether T-tube drainage was instituted (Keighley *et al.*, 1974; Stone *et al.*, 1977). One frequent site of infection after biliary tract surgery is the gall-bladder fossa—also referred to as the right anterior subhepatic space. Although contiguous with other perihepatic, intraperitoneal compartments, pyogenic membrane formation may confine the infection to this region (Meyers, 1977).

Because they are adjacent to the liver, which serves as an excellent "window" for ultrasound examination, gall-bladder fossa abscesses are ideally situated for reliable ultrasonic diagnosis and therapeutic drainage. This paper reports our experience with this complication following biliary tract surgery in three patients.

CASE REPORTS

Patient 1: a 24-year-old man with a three year history of chronic renal failure had a renal transplant in 1973. After surgery, he developed an episode of acute cholecystitis and subsequent cholecystectomy required withdrawal of immunosuppressants and led to eventual transplant rejection. He had been maintained on chronic haemodialysis since that time. Because of symptoms related to jaundice, he was admitted to the hospital on June 1, 1976. Hepatosplenomegaly, scleral icterus, and a mild fever were noted. The patient's liver enzymes were elevated and his total bilirubin was 4.3 mg/100 ml, 4.0 direct. An ultrasound examination on June 7, 1976 revealed a mass in the hepatic portal region. An exploratory laparotomy on June 16 revealed large, noncaseating lymph-nodes (sarcoid) compressing the common bile duct. The nodes were removed and a T-tube was inserted.

One month after discharge, the patient was readmitted because of a two week history of fever, weakness, and diarrhoea. The patient's temperature on admission was 101.8°F and a draining wound was noted at the previous T-tube skin site. Ultrasound examination demonstrated a 5 × 3 × 3 cm

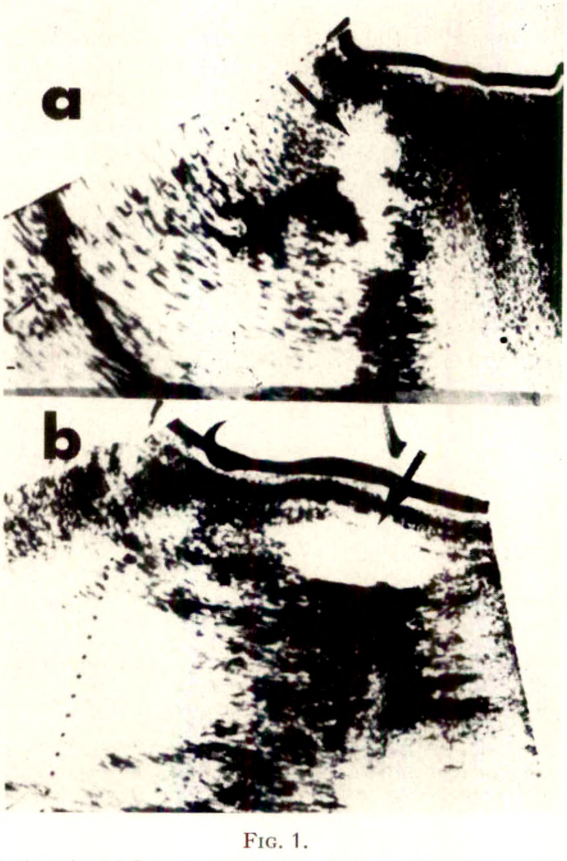

FIG. 1.

Patient 1—(a) Longitudinal scan through the right upper quadrant. The arrow indicates an anechoic fluid collection just inferior to the liver.

Patient 1—(b) Longitudinal scan more medial than Fig. 1a; the collection is quite anterior.

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fluid collection in the gall-bladder fossa (Fig. 1). Open drainage and intravenous antibiotics led to an uneventful recovery and discharge two weeks later.

Patient 2: the patient was a 69-year-old woman who had acute pancreatitis in January of 1976. At that time, an intravenous cholangiogram demonstrated cholelithiasis, but a complicated hospital course, including pulmonary embolism and pneumonia necessitated discharge and readmission in May, 1976, for elective cholecystectomy. The procedure was performed without difficulty except for the incidental finding of a large mass surrounding the transverse colon. The mass, an area of fatty necrosis, was excised. Pathological examination of the gall-bladder showed acute and chronic cholecystitis with cholelithiasis. The bile was sterile.

The patient's recovery was slow, and a low grade fever—attributed to shifting pulmonary atelectasis—persisted until the seventeenth postoperative day. An ultrasound scan demonstrated an 8×4×3 cm fluid collection in the gall-bladder fossa. Closed drainage through a residual T-tube track yielded a large amount of sterile, serosanguineous fluid. A recurrence of fever prompted an exploratory laparotomy revealing a large subphrenic abscess with a fistula to the transverse colon in the area of the fat necrosis excision. Drainage and repair of the colon leak led to prolonged convalescence.

Patient 3: this was a 50-year-old woman who underwent cholecystectomy for acute cholecystitis. Preoperative radiographic studies revealed a normal functioning gall-bladder containing three stones. At surgery, the gall-bladder was thickened. Preoperative cholangiogram revealed a normal common bile duct. The patient did well and was discharged ten days after surgery. Three weeks later she was readmitted because of malaise, epigastric pain, and fever. Physical examination revealed slight tenderness under the right costal margin and epigastrium. Laboratory results were normal except for an elevated sedimentation rate. Ultrasound examination revealed a 2×2×3 cm anechoic, well-demarcated process in the gall-bladder fossa consistent with an abscess (Figs. 2 and 3). Under ultrasound guidance using a biopsy transducer, the suspected abscess was aspirated with an 18 gauge needle, and 12 ml of thick yellow pus was removed. Culture revealed staphylococcus aureus, resistant to penicillin.

The patient received no other therapy and promptly became afebrile and asymptomatic.

Follow up ultrasound examination six weeks after the aspiration was entirely normal (Fig. 4). The patient remains well six months later.

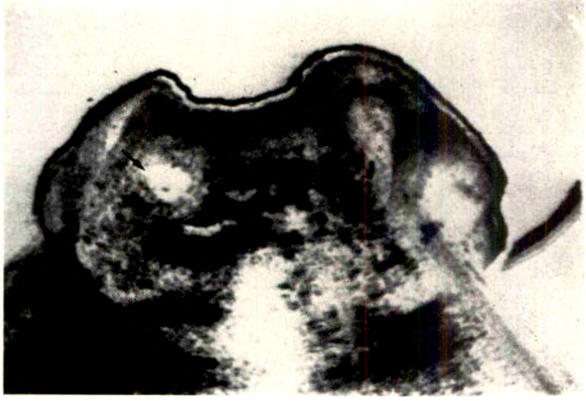

Fig. 2.

Patient 3—Transverse scan showing an anechoic focus (arrow) in the subhepatic region. Needle aspiration revealed an abscess.

Discussion

The efficacy of ultrasound in investigating and localizing suspected intrabdominal abscesses has been demonstrated repeatedly (Berger *et al.*, 1977; Doust and Doust, 1976; Smith, 1975; Smith and Bartrum, 1974), and ultrasound should be considered the primary procedure for this task. This is especially true for the postoperative patient, who may be too ill to withstand more lengthy and invasive studies (McCulloch and Leopold, 1976). As a result, the correct diagnosis should be made soon after clinical symptoms raise the possibility of abscess. This is demonstrated in our patients by comparing the short hospital course of patient 1 with that of patient 2, who experienced fever for two weeks before her gall-bladder fossa abscess was discovered. The high

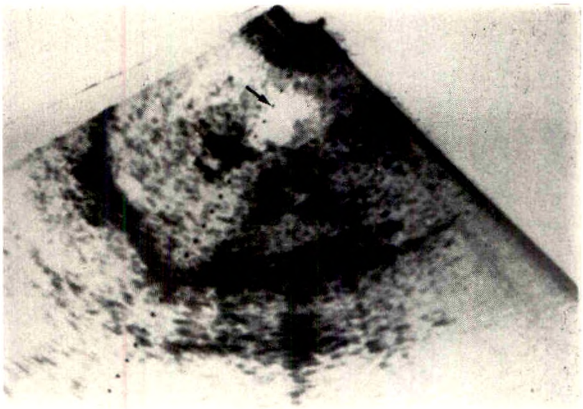

Fig. 3.

Patient 3—Longitudinal scan demonstrating the collection seen in Fig. 2.

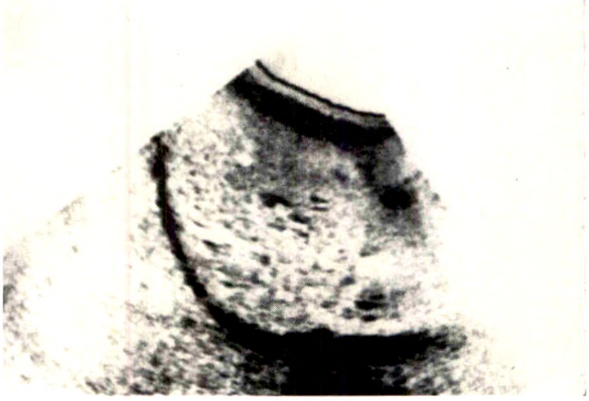

Fig. 4.

Patient 3—Longitudinal follow up scan six weeks after needle aspiration of pus. There has been no recurrence of the abscess.

mortality rate for these lesions and their relative curability by drainage and antibiotic therapy is further impetus for early and accurate diagnosis. In addition, the diagnosis may be confirmed by percutaneous aspiration of the abscess under ultrasound guidance using a special biopsy transducer with a central channel through which a needle can be introduced. This is accomplished with negligible morbidity (Holm *et al.*, 1973; Smith and Bartrum, 1974). Culture of the aspirated material may lead to more appropriate selection of antibiotics, if such therapy is contemplated. In patient 3, complete evacuation of the collection was therapeutic, obviating the need for further surgery, to the relief of both patient and surgeon. The procedure may be slightly modified with the introduction of an indwelling catheter over a guidewire, to be left for long-term drainage (Gronvall *et al.*, 1977).

It would appear that ultrasonic detection and guided drainage in this or any other site may be the logical first step in the approach to suspected localized abscesses. Appropriate antibiotics may be injected directly into the abscess with dramatic results (Ariyama *et al.*, 1978). Should this regimen fail, surgical drainage then may be instituted. Obviously, further experience is needed to confirm this impression.

ACKNOWLEDGMENTS

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REFERENCES

ARIYAMA, J., SHIRAKABE, H., KAYUHIKO, O. and GERAIUT, M. R., 1978. Experience with percutaneous transhepatic cholangiography using the Japanese needle. *Gastrointestinal Radiology*, *2*, 359–365.

BERGER, M., SMITH, E. H., HOLM, H. H. and MASCATELLO, V., 1977. Utility of ultrasound in the differential diagnosis of acute cholecystitis. *Archives of Surgery*, *112*, 273–275.

DOUST, B. D. and DOUST, V. L., 1976. Ultrasonic diagnosis of abdominal abscess. *American Journal of Digestive Disease*, *21*, 569–576.

GRONVALL, J., GRONVALL, S. and HEGEDUS, V., 1977. Ultrasound guided drainage of fluid-containing masses using angiographic catheterization techniques. *American Journal of Roentgenology*, *129*, 997–1002.

HOLM, H. H., RASMUSSEN, S. N. and KRISTENSEN, J. K., 1973. Ultrasonically guided percutaneous puncture technique. *Journal of Clinical Ultrasound*, *1*, 27–31.

KEIGHLEY, M. R. B., LISTER, D. M., JACOBS, S. I. and GILES, G. R., 1974. Hazards of surgical treatment due to microorganisms in the bile. *Surgery*, *75*, 578–583.

MCCULLOUCH, D. L. and LEOPOLD, G. R., 1976. Diagnosis of retroperitoneal fluid collections by ultrasonography. *Journal of Urology*, *115*, 656—659.

MEYERS, M. A., 1977. *Dynamic Radiology of the Abdomen: Normal and Pathologic Anatomy* (Springer-Verlag, New York).

SMITH, E. H., 1975. Ultrasound and abdominal abscesses. *Archives of Surgery*, *110*, 245.

SMITH, E. H. and BARTRUM, R. J., 1974. Ultrasonically guided percutaneous aspiration of abscesses. *American Journal of Roentgenology*, *112*, 308–312.

STONE, A. M., TUCCI, V. J., ISENBERG, H. D. and WISE, L., 1977. Wound infection: acute versus chronic cholecystitis. *American Journal of Surgery*, *133*, 285–288.

Book review

Clinical Radiology of the Ear, Nose and Throat. 2nd Edition. By E. Samuel and G. A. S. Lloyd, pp. 262, illus., 1978 (H. K. Lewis & Co. Ltd., London), £15.

Unlike Europe and North America where there is great interest in otoradiology in particular, ENT radiology is something of a Cinderella in Great Britain. The resultant gap in the home literature has to some extent been filled by this updated version of Professor Samuel's original textbook of 1952. Unfortunately the updating is spasmodic to say the least and only about 10% of the many references are from the present decade. To quote total numbers of recorded cases from series reported in the 1930's seems pointless but there is much resultant confusion over pathology. For instance there can be few cases nowadays of periostitis causing "leontiasis ossium" and most middle ear "angiomas" would be classified as glomus tumours. There are also errors in the text and illustrations several of which simply do not show what the captions state, particularly in the section on the temporal bone. In the subsection on the intracranial complications of sinusitis there is an isolated reference from pre-antibiotic days for the incidence of frontal abscess associated with frontal sinusitis. This is followed by an account of contrast injection into the abscess cavity (pyogram), a technique contra-indicated since the advent of computerized tomography. Sinus neoplasia is well documented with good illustrations but there is more description of the angiographic appearances of antral carcinoma than either conventional tomography or CT.

This is a pity because the book is readable, reasonably priced with a fair overall standard of illustrations. The chapters on the basic radiographic projections are good, particularly the first chapter on sinus views. The last section on the pharynx and larynx is the best part of the book and can be recommended. It is nevertheless hard to see a market for this book. It is too long and specialized to be bought by trainee radiologists or ENT surgeons and it is unsuitable as a reference book because of its many errors and inaccuracies and largely out of date references.

P. D. PHELPS.

1979, *British Journal of Radiology*, *52*, 393–397 May 1979

Radiosensitizing effect of misonidazole in fractionated gamma-ray treatment of a human malignant melanoma grown in athymic nude mice

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(*Received January, 1978 and in revised form December, 1978*)

Abstract

The effect of the hypoxic cell radiosensitizer misonidazole (Ro-07-0582) has been tested on a human malignant melanoma grown subcutaneously in the athymic mutant nude mouse. A ^{60}Co therapy unit was used for local irradiation of the animals. The tumours were exposed daily to 3.75 Gy (375 rad) over four consecutive days, to a total dose of 15.0 Gy. Misonidazole in doses of 500 mg/kg bodyweight was administered intraperitoneally in the mice 45 minutes before each irradiation. The time necessary for the tumours to regrow to their original sizes was compared with that of tumours treated with four daily fractions of 3.75, 4.50 and 5.25 Gy without sensitizer. The enhancement ratio of misonidazole was found to be 1.05.

The presence of small proportions of radioresistant, hypoxic cells in tumours is suggested as a possible cause for local recurrence after conventional radiotherapy (Thomlinson and Gray, 1955). Recently several electron affinic compounds have been shown to be efficient hypoxic cell radiosensitizers *in vitro* (Adams *et al.*, 1971; Chapman *et al.*, 1971; Chapman *et al.*, 1972; Asquith *et al.*, 1974). *In vivo* experiments have indicated that the 2-nitroimidazole, misonidazole (Ro-07-0582), which belongs to this class of compounds, may be of clinical importance. The effect of this radiosensitizer has been tested on a number of murine solid tumours. For large doses of the drug given before a large single dose of X rays, enhancement ratios up to 2.4 and 2.2 have been obtained when tumour cure and tumour regrowth delay respectively were used as a measure of response (for review see Fowler *et al.*, 1976a). The radiosensitizing effect of misonidazole has also been verified clinically. An enhancement ratio of 1.2 was found when subcutaneous metastases from a carcinoma of the uterine cervix were exposed to a single radiation dose of 8.0 Gy (800 rad) (Thomlinson *et al.*, 1976). However, misonidazole will be of particular clinical interest if detectable radiosensitization is obtained when the drug is used in fractionated treatment regimes. Experimental data concerning this aspect are as yet sparse, but those which are obtained from studies of experimental murine tumours indicate that the benefit of misonidazole will depend on both the reoxygenation ability of the tumour and the fractionation regime applied (Fowler *et al.*, 1976a; 1976b).

The present investigation was performed in order to determine the effect of misonidazole upon regrowth delay of a human tumour xenograft subjected to a multiple-dose treatment. A human malignant melanoma growing subcutaneously in the athymic mutant nude mouse was used as test tumour.

Materials and Methods

Mice and tumour

Young male nu/nu/BALB/c/BOM mice were used in this investigation. The animals were kept in a special room at 27°C with automatically regulated 12 hour light and dark periods, under conventional but strict conditions.

The malignant melanoma (EE malignant melanoma) was taken from a lymph node metastasis in the left axilla of a 62-year-old man. Light microscopy examinations showed that the tissue was composed of melanin-poor atypical nevus-cells growing in large balls. Cells and nuclei varied greatly in size and shape. Innumerable mitoses were seen.

Immediately after surgery, one homogeneous piece of tissue was selected from the tumour, cut into cubes approximately 2×2×2 mm in size and inoculated subcutaneously on the dorsal surface of the animals. About one week later the grafts started to grow, and the mice developed non-invasive tumours, histologically indistinguishable from the original tumour material. The tumours consisted of large necrotic areas surrounded by viable, proliferating cells. It is likely that the cells situated closest to the necrotic zones were in a state of hypoxia and thus radioresistant.

Two axes of the tumours were measured with calibrated calipers and the cross-section of the tumours, calculated as being elliptical, was used as parameter for the tumour size. At the day of the first irradiation the tumour cross-sections ranged from 50 to 100 mm^2. Passage 10 of the malignant melanoma was used for the investigation described here.

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*Fellow of The Norwegian Cancer Society.

Radiosensitizer

Misonidazole (1-(2-nitro-1-imidazolyl)-3-methoxy-2-propanol) was obtained as a gift from Roche Products Ltd., Hertfordshire, England. The drug was dissolved in physiological saline immediately before use and administered to the animals by intraperitoneal injection.

A spectrophotometric assay was applied for measurement of serum and tumour concentrations of misonidazole (Urtasun *et al.*, 1977). Immediately before the tumours were dissected free, the blood was collected from the mice in heparinized tubes by heart puncture. Ethanol was added to the blood (9 ml ethanol/ml blood) and to the tumours (9 ml ethanol/g tumour) which had been minced with a scalpel. The samples were centrifuged at 2500 g for 10 minutes and the optical density of the supernatant was measured at 318 nm.

Dosimetry and irradiation procedure

The irradiation procedure has already been described in detail (Rofstad *et al.*, 1977). Only a short description is given here. The mice were irradiated locally without anaesthesia at a focus-skin distance of 80 cm by applying one tangential radiation field from a 5000 Ci ^{60}Co therapy unit (TEM, Mobaltron 80). Acceptable dosimetric conditions were obtained by partly immersing the mouse, placed in a mouseholder, in a water phantom, whereby the entire tumour was positioned under water and at a distance from the outer surface of the phantom wall greater than that corresponding to the ionization maximum of the radiation used. The water temperature was kept at 30°C. Measurements made with thermoluminescent discs (TLD 100 LiF, Ribbon, Harshaw) placed at the ionization maximum varied within a few percent of the corresponding ionization chamber readings of 0.9 Gy/min. The variation of dose within each tumour was determined to be less than 10%.

Experimental design

In a previous investigation with the same malignant melanoma an enhancement ratio of 1.4–1.5 was found when misonidazole in doses of 500 mg/kg bodyweight was injected into the animals 45 minutes before the tumours were exposed to a single gamma-ray dose of 12.5 Gy (Rofstad and Brustad, 1978).

In the present investigation the effect of misonidazole was tested on a multiple dose irradiation regime of four equal daily doses of 3.75 Gy. A total dose of 15.0 Gy, *i.e.* four fractions, was chosen because it was expected to give about the same tumour regrowth delay as that of a single dose of 12.5 Gy. In this way the multiple-dose investigation can better be compared with the single-dose experiment mentioned above. As with the single-dose experiment, misonidazole was administered to the mice in doses of 500 mg/kg bodyweight 45 minutes before each fraction.

The animals were divided into the following groups:

(a) One group receiving 500 mg/kg bodyweight of misonidazole 45 minutes before each daily fraction of 3.75 Gy, over four consecutive days.

(b) Four reference groups, one remaining unirradiated, and three receiving daily fractions without sensitizer of 3.75, 4.50 and 5.25 Gy, over four consecutive days.

RESULTS

The serum and tumour concentrations of misonidazole obtained 45 minutes after intraperitoneal injection of the drug in the mice are shown in Fig. 1. Figure 1a refers to unirradiated mice while Fig. 1b refers to mice exposed to three fractions of 3.75Gy in combination with misonidazole in doses of 500 mg/kg bodyweight over the three previous days. The data in Fig. 1a thus show the concentration level of misonidazole when the mice were ready for the first fraction, while the data in Fig. 1b show the concentration level of misonidazole when the mice were ready for the fourth fraction. The concentration in the tumour at the fourth fraction was about the same as that obtained at the first fraction. During irradiation, the concentration of misonidazole in the tumours was 200–300 μg/g compared with 400–550 μg/ml in the serum.

The mean tumour cross-section of each group of animals as a function of the time after irradiation is shown in Fig. 2. The relative tumour regression following each treatment regime appeared to be independent of the initial tumour cross-section, which ranged from 50 to 100 mm^2. Tumour cross-sections immediately before the first treatment were normalized to unity. The figure reveals that the radiosensitizer causes an additional post-treatment delay (*i.e.* the time from the day the treatment was initiated to the day the tumours had regrown to their original size) of 3–4 days as compared with that of the tumours treated with the same radiation doses but without misonidazole.

Figure 3 shows how the enhancement ratio of the radiosensitizer was determined. The post-treatment delay of the mean tumour size, determined directly

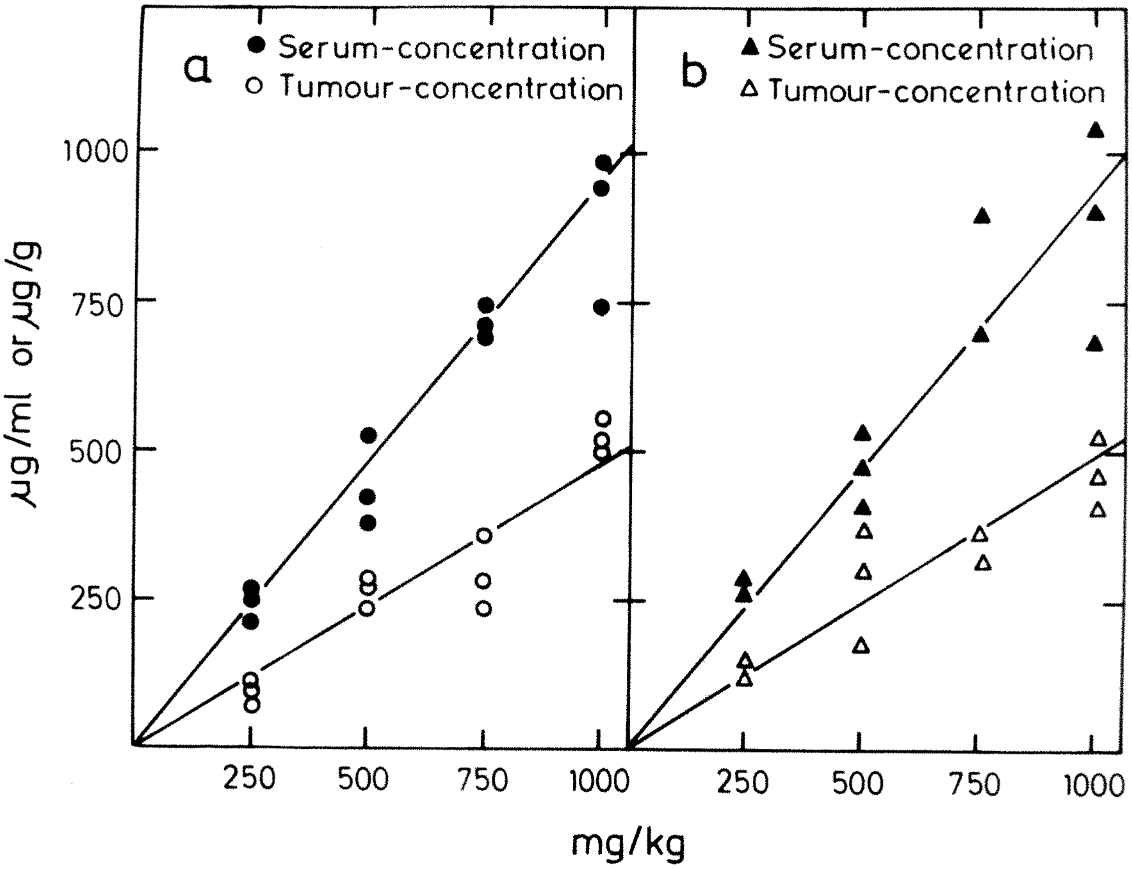

Fig. 1.

Concentration level of misonidazole in serum and in a human malignant melanoma grown in the mutant nude mouse as a function of the amount of sensitizer injected i.p. (mg/kg bodyweight) measured 45 min after injection.

(a) Mice previously untreated.

(b) Mice treated with three fractions of 3.75 Gy in combination with misonidazole in doses of 500 mg/kg bodyweight over the three previous days. This figure thus shows the concentration level of misonidazole pertaining to the time for the fourth and last fraction.

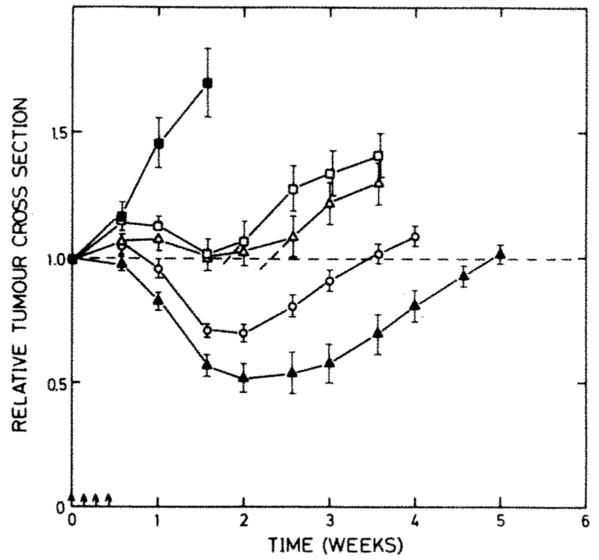

Fig. 2.

Mean relative tumour cross section as a function of the time after the first day of treatment of a human malignant melanoma grown subcutaneously in the mutant nude mouse. The vertical bars indicate the standard deviation of the mean. The arrows symbolize the times at which the treatments were performed.

– ■ – 7 unirradiated tumours.

– □ – 7 tumours treated with 4 fractions of 3.75 Gy.

– △ – 8 tumours treated with 4 fractions of 500 mg/kg misonidazole + 3.75 Gy.

– ○ – 8 tumours treated with 4 fractions of 4.50 Gy.

– ▲ – 7 tumours treated with 4 fractions of 5.25 Gy.

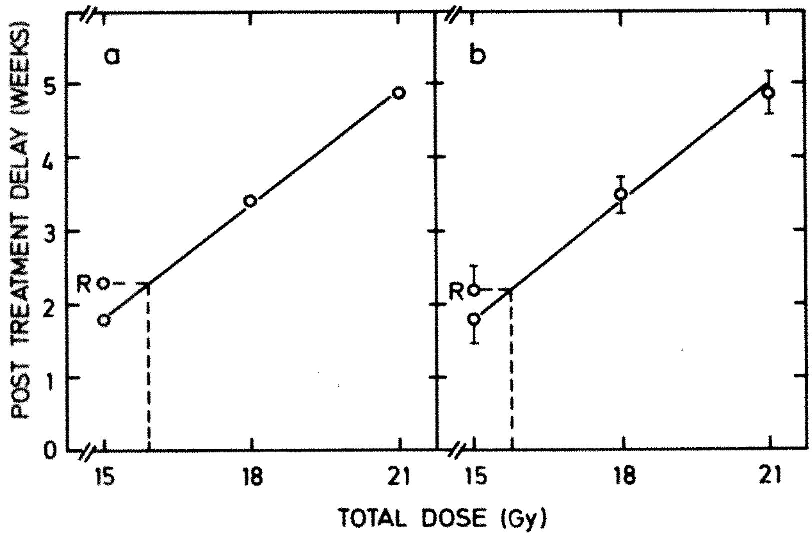

Fig. 3.

(a) Post-treatment delay of the mean tumour size plotted versus total dose for a human malignant melanoma grown in the mutant nude mouse. The total dose was delivered in equal fractions over four consecutive days. (b) Mean post-treatment delay plotted versus total dose for the same experiment as in (a). The vertical bars in (b) indicate the standard deviation of the mean. The symbol R is used to indicate the point showing the effect of the sensitizer misonidazole (Ro-07-0582) in combination with radiation. The dotted lines show how the enhancement ratio of misonidazole was calculated.

from Fig. 2, as a function of total gamma-ray dose appears in Fig. 3a, while in Fig. 3b the mean post-treatment delay of each tumour group, determined from the regrowth curve of each single tumour, is plotted versus total dose. For those tumour groups and single tumours where the size did not fall below the initial value, the post-treatment delay was determined by extrapolation of the regrowth curve, as indicated by the dotted lines in Fig. 2. From Figs. 3a and 3b it can be calculated that the effect of four fractions of 3.75Gy in combination with misonidazole corresponds to that of four fractions of 3.90–3.95 Gy without radiosensitizer, *i.e.* misonidazole exhibits an enhancement ratio of approximately 1.05.

Discussion

In the present study, the hypoxic cell radiosensitizer misonidazole has been used in fractionated irradiation of a human malignant melanoma grown in the athymic mutant nude mouse. A total dose of 15.0 Gy was delivered in daily fractions of 3.75 Gy over four consecutive days, and an enhancement ratio of approximately 1.05 was obtained when misonidazole in doses of 500 mg/kg bodyweight was administered to the animals 45 minutes before each fraction.

The radiosensitizing effect of misonidazole has in several test systems been shown to be dependent on concentration (Asquith *et al.*, 1974; Denekamp *et al.*, 1974). The drug doses used in this investigation correspond to tumour concentrations of 200–300 μg/g during the first as well as the fourth fraction. This concentration level is probably a factor of about two higher than what recent experience would indicate as an acceptable clinical level in a fractionated course of radiotherapy (Dische *et al.*, 1977). With a tumour concentration of misonidazole kept at a clinically acceptable level, an enhancement ratio less than 1.05 is likely to be obtained for this tumour.

Four fractions, each of 3.75 Gy and given over consecutive days, contribute only the first third of a complete clinical fractionation regime to the tolerance level of normal tissue. The present data, therefore, indicate that the benefit of misonidazole is poor in the initial period of such a treatment. Unfortunately, it was not possible to study the effect of misonidazole in a complete fractionation regime because, under the present animal house conditions, the life span of the mice was too short to allow distinction between different complete treatments.

Previously, an enhancement ratio of 1.4–1.5 was found when the same malignant melanoma was exposed to a single dose of 12.5 Gy (Rofstad and Brustad, 1978). Even though the reference treatments in these two experiments, a single dose of 12.5 Gy without radiosensitizer and four daily doses of 3.75 Gy without radiosensitizer, produced approximately identical post-treatment delays, the effect of the sensitizer was greatly diminished when the irradiation was fractionated.

A reduced effect of misonidazole for fractionated irradiation relative to that for single dose irradiation, here demonstrated for the first time for a human tumour xenograft, has previously been shown for mouse tumours (Fowler *et al.*, 1976b). As can be seen from Fig. 1, this reduction is probably not a consequence of poorer penetration of the drug in previously irradiated tumours than in unirradiated tumours.

Clinical data from studies of a majority of tumour types demonstrate that when patients are treated to the same level of normal tissue damage, conventional fractionated irradiation regimes are more effective in eradicating tumours than single doses. This is believed to be due at least in part to the process of reoxygenation taking place in the malignant tissue between the fractions. If this assumption is correct, fractionated irradiation should result in reduced enhancement ratios of misonidazole. Our data are in agreement with this assumption, and they indicate that the malignant melanoma studied here was reoxygenated quite efficiently during the three days which elapsed from the first to the fourth treatment with 3.75 Gy. The present investigation therefore suggests that in the first part of a fractionated course of radiotherapy the dose per fraction should be increased beyond 3.75 Gy if any benefit of misonidazole is to be expected.

If the process of reoxygenation is not completed between each fraction, the enhancement ratio of misonidazole should increase with increasing radiation dose per fraction. This can not of course be proved by the present data, but work in progress, where different daily fractions are used, supports this assumption as well as the general concept of reoxygenation.

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REFERENCES

ADAMS, G. E., ASQUITH, J. C., DEWEY, D. L., FOSTER, J. L., MICHAEL, B. D. and WILLSON, R. L., 1971. Electron affinic sensitization. II. Paranitroacetophenone: a radiosensitizer for anoxic bacterial and mammalian cells. *International Journal of Radiation Biology*, *19*, 575–585.

ASQUITH, J. C., WATTS, M. E., PATEL, K., SMITHEN, C. E. and ADAMS, G. E., 1974. Electron affinic sensitization. V. Radiosensitization of hypoxic bacteria and mammalian cells *in vitro* by some nitroimidazoles and nitropyrazoles. *Radiation Research*, *60*, 108–118.

CHAPMAN, J. D., REUVERS, A. P., BORSA, J., PETKAU, A. and MCCALLA, D. R., 1972. Nitrofurans as radiosensitizers of hypoxic mammalian cells. *Cancer Research*, *32*, 2612–2624.

CHAPMAN, J. D., WEBB, R. G. and BORSA, J., 1971. Radiosensitization of mammalian cells by p-nitroacetophenone. I. Characterization in asynchronous and synchronous populations. *International Journal of Radiation Biology*, *19*, 561–573.

DENEKAMP, J., MICHAEL, B. D. and HARRIS, S. R., 1974. Hypoxic cell radiosensitizers: comparative tests of some electron affinic compounds using epidermal cell survival *in vivo*. *Radiation Research*, *60*, 119–132.

DISCHE, S., SAUNDERS, M. I., LEE, M. E., ADAMS, G. E. and FLOCKHART, I. R., 1977. Clinical testing of the radiosensitizer Ro-07-0582: experience with multiple doses. *British Journal of Cancer*, *35*, 567–579.

FOWLER, J. F., ADAMS, G. E. and DENEKAMP, J., 1976a. Radiosensitizers of hypoxic cells in solid tumours. *Cancer Treatment Reviews*, *3*, 227–256.

FOWLER, J. F., SHELDON, P. W., DENEKAMP, J. and FIELD, S. B., 1976b. Optimum fractionation of the C3H mouse mammary carcinoma using X rays, the hypoxic-cell radiosensitizer Ro-07-0582, or fast neutrons. *International Journal of Radiation Oncology, Biology, Physics*, *1*, 579–592.

ROFSTAD, E. K. and BRUSTAD, T., 1978. The radiosensitizing effect of metronidazole and misonidazole (Ro-07-0582) on a human malignant melanoma grown in the athymic mutant nude mouse. *British Journal of Radiology*, *51*, 381–386.

ROFSTAD, E. K., BRUSTAD, T., JOHANNESSEN, J. V. and MOSSIGE, J., 1977. Effect of cobalt-60 gamma rays and DTIC (5-(3,3 dimethyl-1-triazeno)-imidazole-4-carboxamide) on human malignant melanomas grown in athymic nude mice. *British Journal of Radiology*, *50*, 314–320.

THOMLINSON, R. H., DISCHE, S., GRAY, A. J. and ERRINGTON, L. M., 1976. Clinical testing of the radiosensitizer Ro-07-0582. III. Response of tumours. *Clinical Radiology*, *27*, 167–174.

THOMLINSON, R. H. and GRAY, L. H., 1955. The histological structure of some human lung cancers and the possible implications for radiotherapy. *British Journal of Cancer*, *9*, 539–549.

URTASUN, R. C., BAND, P., CHAPMAN, J. D., RABIN, H. R., WILSON, A. F. and FRYER, C. G., 1977. Clinical phase I study of the hypoxic cell radiosensitizer Ro-07-0582, a 2-nitroimidazole derivative. *Radiology*, *122*, 801–804.

1979, *British Journal of Radiology*, *52*, 398–404

An intercomparison between two methods of obtaining percentage depth doses for irregular shaped fields and comparison of each method with experimental data for ^{60}Co and 10 MV X rays

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Measurements of central ray tissue-air ratio (TAR) for ^{60}Co for a large number of irregularly shaped fields typically encountered in the cancer clinic were compared with TAR values either calculated by the Clarkson method using scatter air ratios or obtained from tables of square field data using the area/perimeter approach. Irregular field shapes included the "L", pentagonal, rectangular, upper and lower mantle and split fields. Agreement between both calculational methods and direct measurement is within ±2% if careful attention is given to central ray position as affected by the proper use of off-centre ratios in air. In the case of 10 MV X rays, eight randomly chosen irregular fields again yielded an average agreement between both methods of calculation and experimental data of less than 1% and an agreement of less than 0.5% between the A/P and Clarkson calculations.

Irregularly shaped fields are commonly used in radiation therapy in order to provide differential dose between healthy and tumorous tissue. Simple geometrical shapes commonly encountered include "L" shaped fields, split fields, pentagonal shaped fields and mantle fields. Other shapes such as yoke fields, lateral skull ("helmet" shaped) fields as well as other possibilities also commonly occur. Frequently, these fields are used in parallel opposed directions although single field protocols may be used in some instances. In any case, it is necessary to calculate a treatment time in the case of ^{60}Co or monitor units (MU) in the case of 10 MV X rays. A choice of parameters such as percentage depth dose, tissue–air ratio (TAR), tissue–maximum ratio (TMR), etc., may be used in the calculations. In this study, the parameter considered is percentage depth dose calculated from experimental TAR data in the case of ^{60}Co teletherapy and TMR experimental data in the case of 10 MV X ray linear accelerator teletherapy. Two basic methods of calculation for irregularly shaped fields are compared in this study and are restricted to the central ray.

METHODS OF CALCULATING PERCENTAGE DEPTH DOSE

In this study, only two procedures were used for determining percentage depth dose, the area/perimeter (A/P) method, and that using scatter function theory. The latter method goes by a variety of names such as "the Clarkson method", "the Cunningham method," "decrement method", etc. In this report, we will refer to it as the Clarkson method since it is simpler and because Clarkson (1941) historically first developed the method in order to change tissue–air ratios obtained from circular beams to values for rectangular beams, *i.e.*, by the use of scatter function theory.

Clarkson method

By means of scatter function theory (Gupta and Cunningham, 1966; Cunningham, 1972; Johns and Cunningham, 1969; Kahn, 1972a; 1972b) one determines the scatter component and the primary component separately. The sum of the two provides the TAR or TMR: thus

$$\mathrm{TMR}=\mathrm{TMR_s}+\mathrm{TMR_0} \qquad (1)$$

$$\mathrm{TAR}=\mathrm{SAR}+\mathrm{TAR_0} \qquad (2)$$

where

TMR is tissue–maximum ratio;

$\mathrm{TMR_s}$ is the scatter component of TMR;

$\mathrm{TMR_0}$ is the primary component of TMR;

TAR is tissue–air ratio;

SAR (scatter–air ratio) is the scatter component of TAR; and

$\mathrm{TAR_0}$ is the primary component of TAR.

On the basis of experimental values of $\mathrm{TMR_0}$ and $\mathrm{TMR_s}$, central ray TMR can be calculated from equation (1) and used to calculate percentage depth dose values using equation (3)

$$\%\mathrm{DD}=\mathrm{TMR}\,[d,(\mathrm{A/P})_d]\times\left(\frac{\mathrm{SSD}+d_{\max}}{\mathrm{SSD}+d}\right)^2\times S(\mathrm{A/P_d},C_d)/S(\mathrm{A/P_t},C_t)\times 100 \qquad (3)$$

where S is the scatter correction for both phantom and collimator, $(\mathrm{A/P})_d$ and $(\mathrm{A/P})_t$ are representative of the phantom scatter component due to field size at depth, d, and $d_{\max}$ ($\sim t$) respectively and C_d and C_t refer to the collimator scatter component at depth d and $d_{\max}$ respectively. We accomplished these calculations by adapting a version of one of Cunningham's programs to an HP 9830A calculator. Percentage depth dose in the case of ^{60}Co is obtainable by calculation from TAR using

$$\%\mathrm{DD} = \mathrm{TAR}\,[d, (\mathrm{A/P})_d] \times \left(\frac{\mathrm{SSD}+d_{\max}}{\mathrm{SSD}+d}\right)^2 \times \frac{100}{\mathrm{BSF}} \quad . \quad . \quad (4)$$

TAR was obtained using the same basic program as that used to obtain TMR except that the scatter correction ratio was replaced by 1/BSF, where BSF is the backscatter factor.

Area over perimeter (A/P) method

This approach is essentially the same as the equivalent square approach where the side of the equivalent square is given by $L = 4 \times (\mathrm{A/P})_0$ where $(\mathrm{A/P})_0$ refers to the area divided by perimeter at the surface of the patient, a convenient parameter when looking up a tabulated percentage depth dose value. When looking up a TAR or TMR, $(\mathrm{A/P})_d$ or area over perimeter at depth is the independent variable and is related to $(\mathrm{A/P})_0$ by $(\mathrm{A/P})_d = (\mathrm{A/P})_0 \times \frac{\mathrm{SSD}+d.}{\mathrm{SSD}}$

In practice (Wrede, 1972a and b) graphs of $(\mathrm{A/P})_d$ (abscissa) versus square field values of TAR, TMR or %DD (ordinate) are plotted for a family of depths. From a knowledge of the area of an irregular shape (found by using a planimeter or by calculating from geometry or by weighing a piece of paper and its perimeter (use of a string, etc.) one can determine the area/perimeter and look up the TAR, TMR or %DD from square-field plots of well established data.

EXPERIMENTAL DATA

TAR measurements for ^{60}Co

Experimental TAR values were determined for 23 rectangular fields, 22 "L" shaped fields, 26 pentagonal fields (Fig. 1), one upper and one lower mantle field as well as a 16×16 cm symmetrically split field and a number of 16×16 asymetrically split fields. A Picker V-9 ^{60}Co teletherapy unit was utilized. Measurements were made in a 40×40×40 cm water phantom using a Shonka-type ionization chamber driven horizontally and vertically by remotely controlled synchronized selsyn motors. The internal volume of the chamber was approximately 0.05 cm^3. "In air" readings were made using a

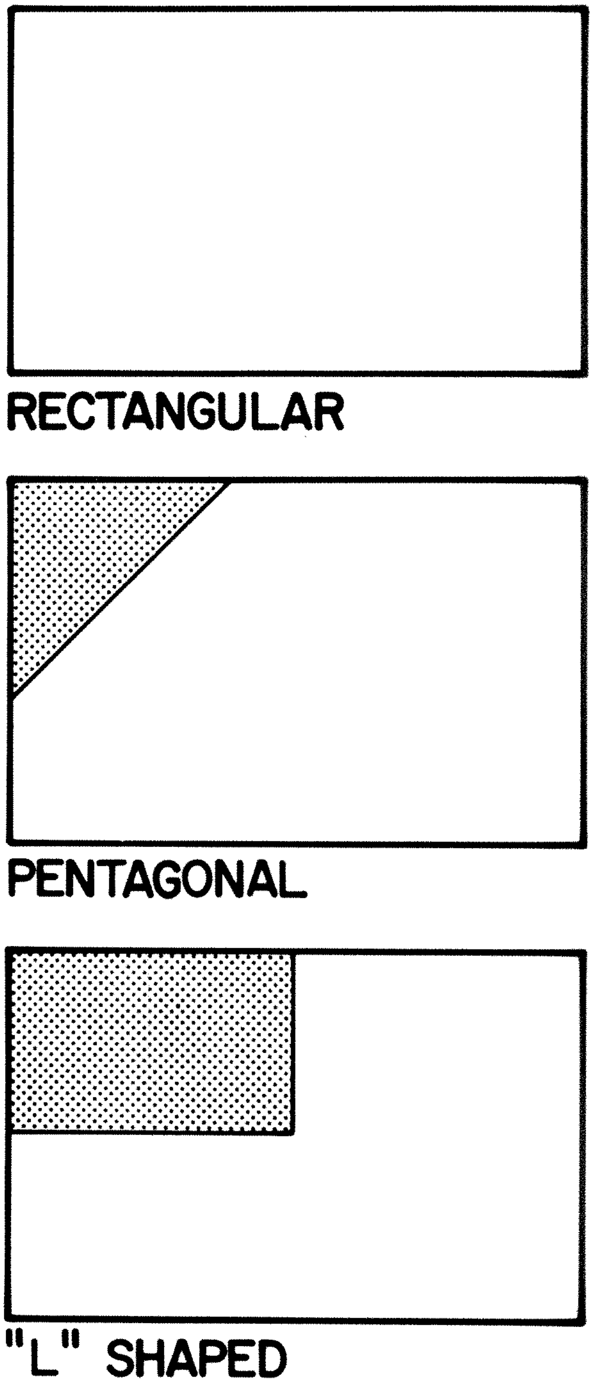

FIG. 1.

Irregular fields for which direct TAR measurements were determined for ^{60}Co. In all cases $(\mathrm{A/P})_0$ is the area/perimeter of the field on the water-phantom surface at an SSD=80 cm. Only the pentagonal and "L" shaped field data are presented in this study for purposes of comparing experimental percentage depth dose values with values from tables.

build-up cap to provide charged-particle equilibrium. Depth was varied from 2 cm to 10 cm in 2 cm increments and collimator settings varied from an extreme of 2 × 36 cm at an SSD of 80 cm to a square of 36 × 36 cm. Readings were obtained on a Keithly model 610B electrometer capable of measurements as small as 10^{-14} A. Scale linearity was determined to be well within ±0.5%.

TMR measurements for 10 MV X rays using square fields

Central ray tissue-maximum ratios were measured directly in an Artonix stand-alone three dimensional water phantom system at depths varying from 0 to 30 cm in 1 cm increments. A Capintec ionization chamber and readout electrometer were utilized. Collimator field sizes were varied from 2 × 2 to

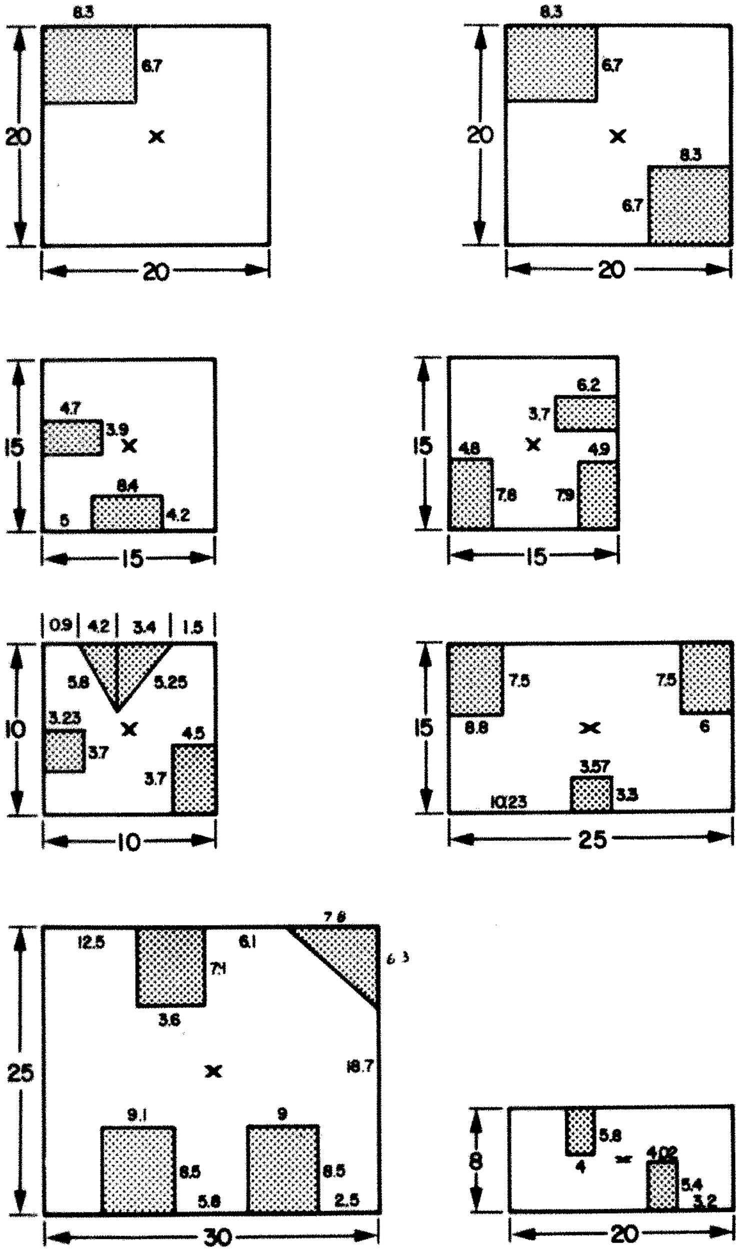

FIG. 2.

Eight randomly chosen irregular fields for which %DD was directly measured for a Varian Clinac-18, 10 MV X ray beam. All fields are for an SSD=100 cm.

30×30 cm as defined at 100 cm. All fields were square and unblocked. These values were stored on cassette tape in the HP 9830A calculator program and formed the basis for the calculation of percentage depth dose according to formula (3).

Percentage depth dose measurements 10 MV X rays and irregular fields

Percentage depth dose measurements were made directly for the eight randomly chosen irregular fields illustrated in Fig. 2 using the 10 MV X-ray beam from a Varian Clinac 18 linear accelerator. Again, a Capintec ionization chamber and readout electrometer were utilized with an Artronix stand-alone three dimensional water phantom system. Measurements were made on the central ray at depths varying from 1 to 20 cm in increments of 1 cm.

RESULTS

Since percentage depth dose for ^{60}Co is directly related to TAR by equation (4) and since TAR values were directly measured, intercomparisons for ^{60}Co TAR's between results from the two calculational methods and the experimental data are shown in Tables I, II and III. In all cases values given by the A/P method and Clarkson's method are compared to the directly measured experimental TAR's and percentage differences are shown. The mean percentage differences in Table I for the "L" shaped fields are only 0.87 and 0.41 respectively for the A/P and Clarkson methods. The average percentage difference between the methods is only 0.46%. In the case of pentagonal shaped fields (data not shown), both methods give TAR's that are 1.94% (A/P) and 1.64% (Clarkson) higher averaged over all the data for the two respective

TABLE I

COMPARISON OF CALCULATED AND MEASURED TAR's FOR "L" SHAPED FIELDS—^{60}Co

$(A/P)_0$	Depth, cm	Measured*	Calculated		Percentage diff., A/P	Percentage diff. Clarkson
			A/P method	Clarkson		
1.0	2	0.944	0.957	0.959	1.4	1.6
	4	0.867	0.875	0.877	0.9	1.2
	6	0.792	0.792	0.793	2.1	2.2
	8	0.695	0.707	0.709	1.7	2.0
	10	0.635	0.630	0.632	0.8	0.5
2.0	2	0.984	0.994	0.993	1.0	0.9
	4	0.916	0.926	0.926	1.1	1.1
	6	0.845	0.854	0.852	1.1	0.8
	8	0.770	0.775	0.774	0.6	0.5
	10	0.700	0.698	0.700	0.3	0.0
3.0	2	1.009	1.015	1.013	0.6	0.4
	4	0.951	0.956	0.953	0.5	0.2
	6	0.882	0.890	0.885	0.9	0.3
	8	0.814	0.818	0.813	0.5	0.1
	10	0.741	0.744	0.740	0.4	0.1
4.0	2	1.020	1.031	1.020	1.1	0.0
	4	0.972	0.973	0.972	0.1	0.0
	6	0.912	0.907	0.911	0.6	0.1
	8	0.851	0.840	0.851	1.3	0.0
	10	0.780	0.765	0.780	2.0	0.0
5.0	2	1.029	1.041	1.029	1.2	0.0
	4	0.985	0.992	0.981	0.7	0.4
	6	0.927	0.932	0.927	0.5	0.0
	8	0.863	0.868	0.863	0.6	0.0
	10	0.794	0.805	0.794	1.4	0.0
6.0	2	1.044	1.050	1.044	0.6	0.0
	4	1.009	1.002	1.009	0.7	0.0
	6	0.942	0.948	0.942	0.6	0.0
	8	0.883	0.888	0.883	0.6	0.0
	10	0.820	0.820	0.820	0.2	0.0
				Average	0.87	0.41

*Five measurements for each field size

TABLE II

TAR VALUES OF AN INVERTED Y FIELD FOR ^{60}Co

Depth, cm	Measured	A/P method	Clarkson method	Percentage difference A/P method × 100 measured	Percentage difference Clarkson method × 100 measured
2	0.987	1.003	1.007	1.6	2.0
4	0.920	0.941	0.946	2.3	2.8
6	0.853	0.868	0.876	1.8	2.7
8	0.783	0.792	0.802	1.1	2.4
10	0.714	0.719	0.726	0.7	1.7
12	0.649	0.649	0.660	0	1.7
14	0.586	0.584	0.599	−0.3	2.2
16	0.528	0.530	0.540	0.4	2.2
18	0.473	0.480	0.484	1.5	2.3
20	0.422	0.432	0.433	2.4	2.6
			Average	1.15%	2.26%

TABLE III

COMPARISON OF TAR'S FOR A 16 × 16 CM UTERINE SPLIT FIELD AT A FIXED DEPTH OF 10 CM FOR ^{60}Co

Region	W_L W_R	Field width	Measured	Calculated		Percentage difference, A/P	Percentage difference, Clarkson
				A/P method	Clarkson method		
1	L	4.25	0.689	0.697	0.671	1.1	−2.7
Symmetrical	R	4.60	0.695	0.703	0.676	1.1	−2.8
2	L	4.65	0.697	0.704	0.677	1.1	−3.0
	R	4.20	0.687	0.696	0.671	1.3	−2.4
3	L	5.10	0.707	0.710	0.683	0.4	−3.5
	R	3.75	0.671	0.684	0.663	1.9	−1.2
4	L	5.60	0.720	0.719	0.688	0.1	−4.7
	R	3.25	0.661	0.674	0.651	2.0	−1.5
5	L	6.15	0.724	0.725	0.697	0.1	−3.9
	R	2.70	0.661	0.658	0.637	−0.5	−3.8
6	L	6.55	0.732	0.730	0.730	−0.3	−4.1
	R	2.30	0.623	0.645	0.629	3.5	1.0
7	L	6.95	0.739	0.734	0.707	−0.7	−4.5
	R	1.90	0.602	0.636	0.616	5.6	2.3
8	L	7.30	0.740	0.738	0.709	−0.3	−4.4
	R	1.55	0.574	0.621	0.605	8.2	5.4

The field is completely split longitudinally with a lead block which casts a shadow 5 cm wide at an SSD of 80 cm. Regions 1 to 8 refer to different positions of the lead block as it is moved from an approximately central position, producing left and right fields of nearly equal size, to the right, producing fields that are asymmetrical relative to the central ray and of unequal size. W_L is the field width on the left of the block and W_R is the field width on the right, the figures given being proportional to the actual dimensions.

methods with a range of variation from 0 to 3.0%. These percentages are somewhat higher than the "L" shaped case relative to the experimental data but when the two methods of calculation are compared, there is, again, only a small percentage difference of 0.30. Tables II and III show results for an arbitrarily chosen lower mantle or inverted Y field and a split 16×16 cm field labelled as "uterine", since our institution commonly uses a field of this size with blocking as part of our protocol for treating uterine carcinoma. These last two fields are mentioned together because they both share one thing in common in our institution, namely an off-centre ratio (OCR), which is dependent on the position of the central ray, and which must be used in the calculation of treatment time or monitor units. In addition, the TAR calculated by the Clarkson method is also dependent on the position of the central ray since the scatter component depends on this position. The importance of OCR and central ray position will be discussed later.

The average percentage difference between the

TABLE IV

Average percentage differences between calculated and measured percentage depth dose values for 10 MV X rays

Field*	Depth variation	Collimator setting	A/P₀†	Percentage differences	
				A/P	Clarkson
1	1–20 cm	20 × 20	4.30	0.24	0.59
2	1–20 cm	20 × 20	3.61	0.32	0.63
3	1–20 cm	15 × 15	2.20	0.50	0.67
4	1–20 cm	15 × 15	1.74	0.72	0.73
5	1–20 cm	10 × 10	1.13	0.47	0.41
6	1–20 cm	15 × 25	2.91	0.06	0.32
7	1–20 cm	25 × 30	3.67	0.38	0.56
8	1–20 cm	8 × 20	1.47	0.35	0.26
			Average	0.38	0.52

*See Figure 2.
†Area/perimeter at surface.

results of the two methods of calculation is 1.1% for the lower mantle inverted Y field of Table II. Although data are presented in Table III for eight different positions of the shielding block, only the symmetrical case (region 1) is used in normal clinical practice for treatment of the pelvic wall. In this case, the A/P approach gives a TAR value which is 1.1% higher than the measured value whereas the values given by the Clarkson method are 2.7% and 2.8% lower for the left and right sides of the field respectively. These differences are well within 1% when the position of the "effective" central ray (centre of the right and left fields) is taken into account (Wrede and Givens, 1977). It should be noted that in the case of the split field data, a TAR (Clarkson) is given by the sum of TAR_0 and SAR, where TAR_0 is the "zero field" or primary component and SAR or scatter air ratio is the scatter component. Since the depth is fixed at 10 cm in this case $TAR_0=0.534$.

In the case of the 10 MV data, the non-irregular TMR data were used to form the data base for the HP 9830A program in order to generate percentage depth dose values for the irregular fields. The actual experimental percentage depth dose values are not shown here but the average percentage differences for the A/P and Clarkson methods relative to the measured values are shown in Table IV. The values given are averages based upon a depth range of 1–20 cm. Clearly the overall average values of 0.38% and 0.52% and the difference of 0.14% are well within experimental error indicating both excellent agreement between the two methods of calculation and their agreement with experimental data.

Conclusions

In our clinic the real central ray is moved to approximately the centre of the area and an off-centre ratio in air (OCR) correction is applied to determine the machine calibrated output at this "effective" central ray position. As an example, consider Table III containing the split field data results. For the symmetrical split field case as indicated by region 1, the OCR (machine dependent) is found to be 0.95 for our cobalt 60 unit. Thus, when calculating tumour dose rate (TDR), we have

$$\mathrm{TDR}=\mathrm{OP}_{80.5}\times\mathrm{OCR}\times\left(\frac{80.5}{\mathrm{SSD}+d}\right)^2\times\mathrm{TAR}$$

where $\mathrm{OP}_{80.5}$=output in rad/min, at 80.5 cm from the source for the particular collimator setting used. If one combines OCR and TAR together in the above case, TAR=0.95 × 0.697=0.662, which when compared to the central ray positional dependent TAR of 0.671 calculated by the Clarkson method gives a difference of 1.36% between the two methods. This is a much closer agreement than the apparent 3.8% difference indicated by Table III. Also, in the case of mantle fields such as the inverted Y in Table II, the TAR values obtained using the Clarkson method are markedly altered by changing the position of the central ray.

In the example shown in Table II there is a difference of 1.1% between the methods but in other cases in the past (using New York Memorial Hospital IRREG Program) we have had no difference in several cases of both lower and upper mantle fields and never had differences greater than ±1%. An upward movement of the central ray by 5 cm in the lower mantle field caused the TAR to decrease by

9%. Our experience with such fields in conjunction with the results indicated in Tables I–III have assured us that either the A/P or Clarkson approach lead to calculated treatment times for ^{60}Co that are in agreement to within ±1% and in agreement with measured values to within ±2% if care is taken to use OCR's and/or to define carefully the position of the central ray for the irregular field. In the case of the irregular field data at 10 MV, our experiments indicate again that either the A/P or Clarkson approach leads to TMR or %DD results that are in agreement with each other to better than 0.5% In conclusion, we believe that either the Clarkson or A/P approach can be used to obtain accurately the dosimetric parameter of interest (TMR, TAR, %DD) for irregular fields on the central ray for ^{60}Co and 10 MV X rays and that the preferred choice is dependent on the availability of equipment such as planimeters, digitizers, calculators, computer equipment, etc. In the case of off-axis calculations in irregular fields, off centre ratios in tissue can be used but the Clarkson method is preferable since the approach using OCR in tissue has not been fully demonstrated in the literature to give equivalent results with irregular fields. The results in this study are compatible with those of Kahn *et al.* (1972b) who state "it is reasonable to assume the radius of an equivalent circle is equal to one-half the side of the equivalent square" with high energy X rays as well as with those of Tsung (1977), and show that the A/P method and Clarkson method agree even more closely at higher energies. This is probably due in part to the fact that the variation of percentage depth dose with field size is decreased at higher energies as compared with ^{60}Co.

REFERENCES

CLARKSON, J. R., 1941. A note on depth doses in fields of irregular shape. *British Journal of Radiology, 14*, 265.

CUNNINGHAM, J. R., 1972. Scatter air ratios. *Physics in Medicine and Biology, 17*, 42–51.

GUPTA, S. K., and CUNNINGHAM, J. R., 1966. Measurement of tissue air ratios and scatter functions for large field sizes for cobalt 60 gamma radiation. *British Journal of Radiology, 29*, 7–11.

JOHNS, H. E., and CUNNINGHAM, J. R., 1969. *The Physics of Radiology*, 3rd edition (Charles C. Thomas), 323–325.

KHAN, F. M., 1972a. Computer and approximation methods of calculating depth dose in irregular shaped fields. *Radiology, 106*, 433–436.

KHAN, F. M., MOORE, V. C., and SATO, S., 1972b. Depth dose and scatter analysis of 10 MV X rays. *Radiology, 102*, 165–169.

TSUNG, P., 1977. A method of dose calculation for rectangular port fields for 8 and 25 MV photon beams; presented at the fourth international conference on medical physics. *Physics in Medicine and Biology, 22*, 569.

WREDE, D. E., 1972a. Central axis tissue air ratios as a function of area/perimeter at depth and their applicability to irregularly shaped fields. *Physics in Medicine and Biology, 17*, 548–554.

1972b. Technical note: practical aspects of area/perimeter. *AAPM Quarterly Bulletin, 6*, 73–74.

WREDE, D. E., and GIVENS, S. B., 1977. Dosimetric considerations of symmetric and asymmetric ^{60}Co teletherapy split fields. *Medical Physics, 4*, 437–440.

Book reviews

The Mediastinum. Radiologic correlations with anatomy and pathology. By Robert E. Heitzman, pp. xi+341, illus., 1977, (C. V. Mosby Co., St. Louis), $37.50.

Many radiologists will already be familiar with Dr. Heitzman's earlier companion volume on the lung. They will not be surprised at the quality of this book. The emphasis is on a thorough understanding of anatomy. Cadaver body sections are correlated with radiographs and CT scans. The upshot is a clear demonstration of mediastinal radiographic anatomy and how this may be affected by various diseases. Many radiologists will recognize some of the lines and shadows described here. They will now know what they represent. I have certainly had some of the scales removed from my own eyes and would suggest that other people with an interest in chest disease subject themselves to the same pleasure. The book is easy to read and if you still do not believe everything there are enough references to keep you going well into the night. All departmental libraries would benefit from a copy of this book.

C. D. R. FLOWER.

Atlas der Nierenangiographie. By P. Meiisel and D. E. Apitzsch, pp. 201+336 illus., 1978 (Springer Verlag, Berlin-Heidelberg-New York), DM148.
ISBN 3-540-08486-X.

This is an excellent atlas of renal angiography. The text is short, and therefore necessarily didactic, even take-it-or-leave-it. A basic aquaintance with angiographic technique is taken for granted. The illustrations (black on white, *i.e.* reversed) are the book's chief glory. They are stunningly well done. When will a British publisher rival this quality?

Most renal disorders of angiographic interest are illustrated. Inevitably there are a few worries. Chronic pyelonephritis the most frequent kidney disease (p. 63)? The mention of mythical "Bertini" on p. 1 does not augur well for getting things right about the course of the interlobar/arcuate arteries in relation to the renal lobe and the septa of Bertin (see Hodson's work). These are small niggles about a fine atlas for German-speaking departments.

THOMAS SHERWOOD.

1979, *British Journal of Radiology*, 52, 405–408

Technical notes

Effervescent granules for the barium meal

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(*Received July, 1978*)

The double contrast barium meal has recently become the routine examination in many departments (Kreel *et al.*, 1973; Scott-Harden, 1976). However, the examination does present some technical difficulties, and one of these is the production of gas (James *et al.*, 1976; Lintott *et al.*, 1978). Effervescent agents are most commonly used, and Baritop† tablets and Carbex‡ granules are two preparations marketed in the U.K. specifically for this purpose. Other effervescent products such as Redoxon, Calcium-Sandoz or Andrews Liver Salts are used by some radiologists.

The main requirements of a gas-producing agent are: release of an adequate volume of gas (200–400 ml), non-interference with barium coating, absence of bubbles, rapid disintegration leaving no residue, ease of swallowing and low cost. None of the above products completely fulfills all these requirements. Redoxon and Calcium-Sandoz generate a high level of foam which can adverseley affect coating. The Carbex preparation is a rapid and efficient method of producing carbon dioxide but it is relatively expensive, and dilution of low density barium suspensions by the citric acid solution may occur. With the very dense media (170% w/v) this is not a problem, but with preparations such as Baritop 100 (100% w/v), poor coating may result. Baritop tablets are also relatively expensive, and we have occasionally experienced two particular difficulties with this preparation. Firstly, undissolved tablets were seen on films and could be misinterpreted as ulcers or polyps (Fig. 1); and secondly, inadequate gas production occurred even when the number of tablets used was above the recommended dose of 20–30. This study was carried out to determine the cause of these difficulties and also to produce our own effervescent granules in the hospital pharmacy.

DISSOLUTION RATES OF BARITOP TABLETS

To discover whether batch to batch variation in dissolution rates occurred, a single tablet from each of three batches was disolved in 50 ml of distilled water maintained between 37° and 39°C, and the time taken for dissolution noted. Five determinations were made for each batch and the corresponding mean dissolution times (MDT) were obtained. The experiment was repeated using lots of five tablets and an MDT per five tablets was obtained for each batch. Large variations in MDT values for both single tablets and lots of five tablets were observed between the different batches (Table I). In addition it can be seen that the MDT for the single tablet was always less than the MDT for the coresponding lot of five tablets in a given batch. During dissolution a scum of antifoam formed on the surface of the water, and the production of Co_2 forced the tablets to the surface of the liquid where they remained and were inadequately wetted. This effect was thought to be the cause of the increase in MDT's for lots of five tablets as compared with those for single tablets. A subsequent experiment was therefore devised to determine if this were so. A single batch (2116) was used in this determination. Five tablets were dissolved in 50 ml of distilled water maintained between 37° and 39°C, and time taken for dissolution noted. A second lot of five tablets was then introduced into the same 50 ml of water and the time for dissolution again recorded. This was repeated until a total of 30 tablets had been dissolved. The dissolution times for each lot are given in Table II. These results show that the dissolution time per five tablets increases as more tablets are dissolved, and this effect

TABLE I

MEAN DISSOLUTION TIMES (MDT) FOR DIFFERENT BATCHES OF BARITOP TABLETS IN 50 ml WATER AT 37°C

Batch No.	2116*	8070	0300
MDT per five tablets	37·18 s	31·58 s	72·30 s
MDT for single tablets	36·58 s	26·60 s	71·56 s

*This batch used for subsequent experiments.

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†Concept Pharmaceuticals Ltd., London.

‡Ferring Pharmaceuticals Ltd., London.

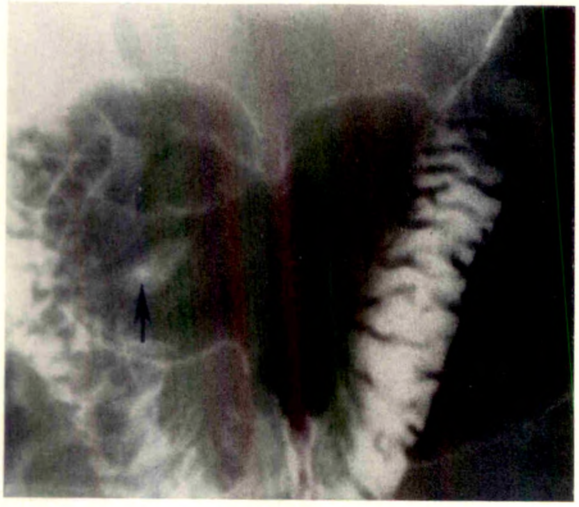

FIG. 1.
Undissolved Baritop tablet in the stomach.

TABLE II

DISSOLUTION TIMES FOR INCREASING NUMBERS OF BARITOP TABLETS IN 50 ml WATER AT 37°C. (ALL TABLETS FROM BATCH 2116)

	Determination I	Determination II
Five tablets in 50 ml of water	38·8 s	44·8 s
1st addition of five tablets	45·0 s	48·4 s
2nd addition of five tablets	50·2 s	50·2 s
3rd addition of five tablets	57·3 s	58·0 s
4th addition of five tablets	62·8 s	61·0 s
5th addition of five tablets	70·0 s	72·0 s

TABLE III

DISSOLUTION TIMES FOR FIVE BARITOP TABLETS MIXED WITH VARIOUS MEDIA IN 50 ML WATER AT 37°C. (ALL TABLETS FROM BATCH 2116)

	Determination		
Medium	I	II	II
Water control	38·8 s	44·8 s	—
Mylocon	57·8 s	56·5 s	57·5 s
Baritop 100 (100% w/v)	50·0 s	52·5 s	49·5 s
EZ HD III (170% w/v)	45·8 s	46·5 s	47·8 s
EZ PAQUE (170% w/v)	50·5 s	49·8 s	47·0 s

TABLE IV

DISSOLUTION TIMES FOR 15 BARITOP TABLETS IN 50 ML OF VARIOUS MEDIA AT 37°C. (ALL TABLETS FROM BATCH 2116)

	Time for dissolution	
Medium	I	I
Water control	47·5 s	54·0 s
Baritop 100 (100% w/v)	12 m 1 s	13 m 48 s
EZ HD III (170% w/v)	30m	30 m
EZ–PAQUE (170% w/v)	30 m	30 m
Mylocon	7 m 48 s	—

is attributed to the scum formation. This scum consisted of dimethicone (3 mg per tablet) and it is considered that this hindered the wetting and dissolution of the tablets.

In order to assess the effect of different commercial barium preparations and a silicone antifoaming agent on tablet dissolution the following two experiments were then performed. First, using the beaker method previously described, a lot of five tablets was mixed into a slurry with the appropriate medium and poured into 50 ml of distilled water maintained between 37° and 39°C. The dissolution time was noted. Table III gives the results of three determinations per medium which shows that all the media investigated increased dissolution times. Two of the media, E–Z HD III (170% w/v) and EZ PAQUE (170% w/v) sank to the bottom of the beaker and released the tablets which were then free to dissolve. Second, using a similar technique, the dissolution times for lots of 15 tablets in 50 ml of pure medium maintained between 37° and 39°C were determined. Determinations were performed twice for each medium and the results are shown in Table IV. All undiluted media severely restricted dissolution; with the high density media E–Z HD III and EZ PAQUE dissolution was effectively halted since the tablets merely floated to the top of the medium and did not dissolve. Two main points emerge from consideration of these results. Dissolution of tablets is hindered by the presence of silicone antifoam, such as mylocon and dimethicone, and dissolution is further hindered with high density barium suspensions such as EZ PAQUE and E–Z HD III. Thus undissolved Baritop tablets are most likely to occur in clinical practice when using a large number of tablets, from a batch with a long dissolution time, a high density medium to wash them down, in a patient with very little resting juice. In these circumstances not only may undissolved tablets be seen on the films, but the volume of gas produced in the stomach will appear disproportionate to the number of tablets ingested.

Formulation of Effervescent Granules in the Hospital Pharmacy

O'Reilly and Bryan (1974) developed a method of gas production which worked adequately with Barosperse barium. The method utilized separate suspensions of citric acid and sodium bicarbonate in large volumes of the barium suspension. The main disadvantages with this system are that the preparation of these suspensions is time consuming, they are stable for only one week, and must be stored in a refrigerator. Hunt and Anderson (1976) described a sodium bicarbonate/citric acid powder, which is easily prepared but difficult to swallow because of insufficient granulation.

The pharmacy at this hospital undertook the production of a cheap and efficient gas producing agent compatible with a wide range of barium preparations. It was thought that the best presentation would be effervescent granules large enough to be swallowed when dry. The granules were prepared by intimately mixing citric acid and sodium bicarbonate powders in a mortar and heating in a flat dish on a boiling water bath. A little water of crystallization is liberated from the citric acid rendering the mixture moist and coherent. The mass is then forced through a number 10 mesh sieve to produce large granules of a uniform size which are then dried at a temperature not exceeding 55°C.

The granules were found to provide a satisfactory volume of gas, (200 ml gas/20 g dose). Icing sugar was incorporated for sweetening, but the quantity required to improve the taste hardened the pre-granulation mass leading to unsatisfactory sieving. Saccharin was tried as an alternative, and no hardening was experienced but an unpleasant after-taste was noted. A satisfactory compromise was achieved by using a mixture of saccharin and icing sugar. The granules were not bitter but had an acidic taste, and in order to improve this, three different flavouring agents were tried. These were peppermint oil, which masks the acidic taste and lemon oil and orange spirit both of which complement it. The lemon flavoured granules were the most palatable. On using these granules for barium examinations, it became apparent that because of bubble formation within the barium, an antifoaming agent was required. Administration of Mylocon gave satisfactory results, but for patients' convenience and ease of administration it was decided to incorporate an antifoaming agent in the granules. Silicone fluid MS 550 in absolute alcohol was added to the dry powders prior to granulation. On heating the mixture the alcohol evaporated leaving the silicone fluid evenly dispersed. The final formula for the granules is as follows:

Sodium bicarbonate	475 g
Citric acid	200 g
Tartaric acid	230 g
Icing sugar	90 g
Saccharin sodium	125 mg
Silicone MS 550	20 ml
Lemon oil	6·25 ml
Absolute alcohol	50 ml

Comments in Regard to the use of Gas Producing Agents

When Baritop tablets are used, the following points should be considered. If using a less viscous barium *e.g.* Baritop (100% w/v), the tablets may be washed down with the medium, providing that an excessive number of tablets are not taken. With the more viscous barium suspensions (EZ PAQUE at 170% w/v), the tablets should be swallowed with a small quantity of water, and time allowed for complete dissolution before drinking the barium. When Carbex is used, the granules are easily swallowed using the citric acid solution, releasing gas rapidly and in a reliable volume. There appear to be no adverse effects on mucosal coating when used with high density barium suspensions. The simple method of gas production using Barosperse suspensions (O'Reilly and Bryan, 1974) does not appear to have been tried with other bariums. Crushed proprietary tablets/powders are not recommended, even though these will produce large volumes of gas and are easily swallowed, there is excessive foaming and bubble formation which are disadvantageous. Field* Gas Producing Liquids, or X-Evess† Effervescent Powder are Australian preparations which should be available in the UK in the near future. Though these products are usually used in conjunction with either the Field* or Forrest† barium they are equally effective with other barium suspensions presently available.

Finally, when using the St. George's Hospital effervescent granules, our protocol is as follows: the waiting patient is given the granules (20 g which is one heaped tablespoonful) in a small beaker and chews or swallows them while waiting outside the

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*Field Group Chemicals Pty. Ltd., Sydney, N.S.W.

†Forrest Pharmaceutical Co. Pty. Ltd., Sydney, N.S.W.

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fluoroscopy room. If there is difficulty in swallowing the granules then 10 ml of water is given to wash them down. The patient enters the room and after an intravenous injection of 20 mg of Buscopan he is lain supine and screened to see if enough gas is present in the stomach. If there is enough gas (four out of five patients) then the patient swallows the barium and the examination proceeds in the sequence described by de Lacey (1976). If there is too little gas present on screening (the patient may have released part of it) then Carbex granules and solution are given because of their rapid and reliable gas release.

It is not suggested that our granules necessarily represent the optimal method of gas production. Indeed it is probable that the best methods are those in which the manufacturers have prepared an effervescent formula tailored to their own barium suspension. The two Australian manufacturers, Forrest† and Field* have prepared such systems, both of which are simple, easy to use, and take into account the intimate relationship between the barium and the other components of the double contrast examination. Nevertheless for those radiologists for whom such a combination is not yet available, our formulation provides an alternative which compares favourably with the commercial granules and tablets presently marketed in the UK.

ACKNOWLEDGMENTS

Our thanks to Dr. Giles Stevenson of McMaster University Medical Centre and Dr. John Hunt of the Royal North Shore Hospital of Sydney, who provided the stimulus for us to seek a method of granulating an effervescent powder; and also to the Pharmaceutical Department of St. George's Hospital for the formulation and production of the granules.

REFERENCES

DE LACEY, G. J., 1976. The double contrast barium meal. *Ilford X-ray Focus*, *15*, 43–50.

HUNT, J. H. and ANDERSON, I. F., 1976. Double contrast upper gastro-intestinal series. *Clinical Radiology*, *27*, 87–97.

JAMES, W. B., MCCREATH, G., SUTHERLAND, G. R., and MCDONALD, M., 1976. Double contrast barium meal examination—a comparison of techniques for introducing gas. *Clinical Radiology*, *27*, 99–101.

KREEL, L., HERLINGER, H., and GLANVILLE, J., 1973. Technique of the double contrast barium meal with examples of correlation with endoscopy. *Clinical Radiology*, *24*, 307–314.

LINTOTT, D. J., SIMPKINS, K. C., DE DOMBAL, F. T., and NOAKES, M. J., 1978. Assessment of the double contrast barium meal: method and application. *Clinical Radiology*, *29*, 313–321.

O'REILLY, G. V. A. and BRYAN, G., 1974. The double contrast barium meal—a simplification. *British Journal of Radiology*, *47*, 482–483.

SCOTT-HARDEN, W. G., 1976. Upper digestive tract radiology today. *British Journal of Radiology*, *49*, 658–659.

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The value of cimetidine in routine barium meals

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(*Received July 1978*)

The double contrast barium meal is one of the commonest investigations of the stomach and duodenum. Its success depends on good coating of the gastric mucosa with barium. The features which affect mucosal coating are not completely understood. Gastric secretions might be expected to decrease mucosal coating by diluting barium and also by forming a physical barrier between the barium and the stomach wall. Cimetidine is a potent inhibitor of gastric acid secretion (Editorial: British Medical Journal 1976; Lancet 1974). After a single dose its effect is rapid and powerful (Henn *et al.*, 1975). Its effect on mucus secretion is less well known. Could a reduction in gastric secretion by cimetidine improve the diagnostic quality of barium meals?

METHODS

One hundred and ten consecutive patients referred for barium meal examination to the Leeds General Infirmary X-ray Department were studied. Twelve patients were excluded who had pernicious anaemia, previous gastric surgery, were already on cimetidine, or who vomited after taking tablets. Patients were randomly allocated into two groups, receiving either tablets of ascorbic acid or cimetidine (200 mgms tablet). They took two tablets (400 mgm) approximately 15 hours and a further two tablets (400 mgm) approximately three hours before their examination. The study was double blind.

All the examinations were performed by the same person. A conventional double contrast barium meal

TABLE I

Barium coating of mucosa and visibility of areae gastricae in 98 patients. The scores are mean values from three observers

	No.	Barium coating of mucosa (Mean ± S.E.)	Visibility of areae gastricae
Patients receiving ascorbic acid	40	45.15 ± 1.7	28.05 ± 19.6
Patients receiving cimetidine	48	56.04 ± 17.6	32.83 ± 23.2

was used. Easipaque barium was used in all cases. Each patient received Carbex to produce gas in the stomach. Buscopan (20 mgm intravenous) was given to every patient at the start of the examination.

Coating of mucosa and areae gastricae was evaluated by three observers by the method of Lintott *et al.*, (1978), giving each parameter a score out of 100 on the linear analogue scale. The results are shown in Table I.

Discussion

There has been only one previous study of the value of cimetidine in routine barium meals (James *et al.*, 1977). They used similar doses of cimetidine to the present study and also a double contrast barium meal. They included only 49 patients in their study. Although their results suggested that cimetidine was not of value, their numbers were too small to permit statistical analysis.

The present study showed that although the patients receiving cimetidine scored better for mucosal coating and visibility of areae gastricae than the control group, the differences are *not* statistically significant ($P > 0.05$). It is thus concluded that cimetidine in the doses used, has no value in the routine barium meal. It may be that mucus, rather than hydrochloric acid, is a major factor reducing barium coating of the stomach. Mucus has been shown to reduce mucosal coating in the pigs stomach (Mackintosh and Kreel, 1977). While cimetidine is a potent inhibitor of acid secretion, its effect on mucus secretion may be much less.

Acknowledgments

I wish to thank Dr. K. Simpkins and Dr. D. Lintott for evaluating all the barium meals and Dr. T. De Dombal for statistical assistance.

REFERENCES

Editorial, 1976. Histamine antagonists and peptic ulcer. *British Medical Journal*, *1*, 789–790.

Editorial, 1974. Gastric acid, ulcers and H_2 receptors. *Lancet 1*, 666–667.

Henn, R. M., Isenberg, J. I., Maxwell, J., Sturdevant, A. L., 1975. Inhibition of gastric acid secretion by cimetidine in patients with duodenal ulcer. *New England Journal of Medicine*, 293, 371–375.

James, W. B., Standton, B., Teasdale, E., and McCreath, G., 1977. The effect of cimetidine on barium coating of the gastric mucosal. *British Journal of Radiology*, *50*, 445–446.

Lintott, D. J., Simpkins, K. C., De Dombal., F. T. and Noakes, M. J., 1978. Assessment of the double contrast barium meal: method and application. *Clinical Radiology*, *29*, 313–321.

Mackintosh, C. E., and Kreel, L., 1977. Anatomy and radiology of the areae gastricae. *Gut*, *18*, 855–864.

Book review

Motilität der oberen Harnwege. Radiologische Diagnostik und Literaturübersicht. By Hermann Schmidt, pp. 120 + 71 illus., 1978 (Springer Verlag, Berlin/Heidelberg/New York) DM68.

ISBN 3-540-08612-9

This slim volume is a careful account of many years' experience in screening the upper urinary tracts during IVUs. The author has clearly dug deep into the voluminous literature on his subject, and indeed such a review is a part of the purpose of his book. Then there are his own observations, with particular attention to the various disturbances of motility he considers important, *e.g.* reverse ureteric peristalsis. It is a piece of work in the grand tradition of descriptive medicine: only observe and read the book of nature patiently, and in time all will be revealed to you. In keeping with this stance the volume is written mainly in the passive voice. The preface by Prof. Diethelm says that this is important work which deserves the utmost attention of radiologists, urologists, nephrologists, paediatricians and gynaecologists. That may well be so, though many radiologists in this country will not need convincing that screening the upper urinary tracts during an IVU can quickly resolve various problems, *e.g.* nailing a doubtful ureteric stone. The now established practice of antegrade (percutaneous) pyelography with fluroscopy/pressure measurements is perhaps especially good at illuminating the more difficult problems in Prof. Schmidt's field. Interested readers will wish to sample this book, but it is rather expensive even for inflated British pockets.

Thomas Sherwood.

1979, *British Journal of Radiology*, *52*, 410–411

Case reports

Pulmonary oedema following intravenous urography in a neonate

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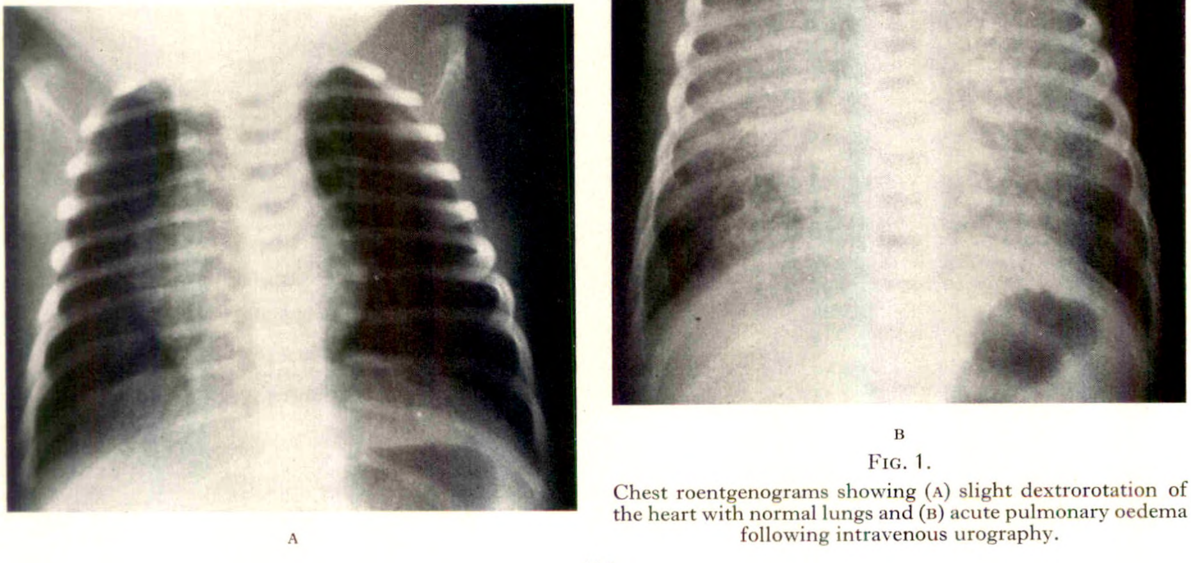
The quantity of contrast agent that should be used for intravenous urography for neonates has been consistently higher than that for older children and adults. The authors wish to report an 18-day-old girl who developed pulmonary oedema shortly after receiving 4.7 ml/kg of Hypaque 50, a dose within the range recommended in some publications (Henderson and Torch, 1977; Standen *et al.*, 1965).

CASE HISTORY

A 3 kg newborn girl who was the product of an uneventful pregnancy and delivery, was admitted to St. Louis Children's Hospital for exstrophy of the bladder, imperforate anus, and a small omphalocele. The omphalocele was repaired the first day of life and a colostomy performed. A chest roentgenogram demonstrated only slight dextroversion of the heart (Fig. 1A). She was clinically stable and well hydrated without unusual fluid loss from the colostomy. On day 17 the patient's serum chloride, sodium, potassium and blood urea nitrogen were normal. On day 18 the patient had an unprepared intravenous urogram. Fourteen ml (4.7 ml/kg) of Hypaque 50 (sodium diatrizoate) was injected through a 23 gauge needle. The length of time of injection was under one minute. A few minutes following the injection, the patient became cyanotic, and had bloody frothy sputum, tachycardia and tachypnoea. Auscultation revealed bilateral rales and rhonchi. The clinical diagnosis was pulmonary oedema, and the patient was treated with oxygen, semi-erect position, and intravenous digitalization. A chest roentgenogram 20 minutes following injection of the contrast agent confirmed pulmonary oedema (Fig. 1B). An abdominal roentgenogram several hours later showed normal kidneys. A chest roentgenogram the following day showed virtually complete clearing of the pulmonary oedema. The patient continued to do well, and clinical and laboratory cardiac evaluation were normal. Subsequent intravenous urography has been performed without difficulty.

DISCUSSION

The type of adverse response in our patient suggests overdosage by a hypertonic contrast medium with resultant cardiopulmonary failure from increased intravascular volume. Previous investigators (Bernstein *et al.*, 1961; Busfield *et al.*, 1962; Lachlan, 1970; Lindgren *et al.*, 1968; Mudd *et al.*, 1965; Sotos *et al.*, 1962; Standen *et al.*, 1965) have



A

B

FIG. 1.

Chest roentgenograms showing (A) slight dextrorotation of the heart with normal lungs and (B) acute pulmonary oedema following intravenous urography.

shown profound rapid changes in patients and experimental animals in serum osmolarity, pH, electrocardiography, heart rate and blood pressure, following the injection of urographic agents or hypertonic agents. A coincidental fall in haematocrit in experimental animals also occurs, indicating that fluid was being rapidly drawn into the vascular compartment.

Fatal cardiopulmonary reactions in infants and children have been reported with overdoses in the range of 7 to 9 ml/kg or greater. One was a newborn infant (weight 2.1 kg at the time of urography) who died of cardiopulmonary failure soon after receiving 7.0 ml/kg of Conray 60 (meglumine iothalamate) (McClennan *et al.*, 1972). Ansell (1970) reported three other infants dying from overdoses of intravenous contrast agents. The amount of urographic agent received in these three patients was (1) 250 ml of 30% Urografin (80 ml/kg) meglumine and sodium diatrizoate; (2) 25 ml of Urovison (8 ml/kg) (meglumine and sodium diatrizoate); and (3) 20 ml of Urografin (6 ml/kg) repeated after ten minutes. A 3.7 kg infant developed reversible cardiac arrest and pulmonary oedema after receiving 3.3 ml/kg of 45% sodium diatrizoate (Ansell, 1976). Pulmonary oedema has been reported in adults receiving contrast media (Malins, 1978; Shehadi, 1975).

Deaths in experimental animals from the commonly used monomeric intravenous contrast agents (Hypaque 50, Conray 60, and Renografin 60) has been reported with doses ranging from 6.8–19 ml/kg and higher (Bernstein *et al.*, 1961; Busfield *et al.*, 1962; McClennan *et al.*, 1972; Salvesen, 1973). The wide range of toxicity values in experimental animals largely reflects differences in rates of injection of the contrast agents (Busfield *et al.*, 1962; Hoppe, 1959; Salvesen, 1973). Busfield *et al.* (1962) in their experiments on rats almost doubled the LD_{50} levels by slow injections. In newborn rats the LD_{50} of Hypaque 50 is 10 ml/kg, one half that of the adult rat (Kaufman *et al.*, 1966). The LD_{50} of dogs receiving Hypaque M90 rapidly injected was 3 ml/kg and death resulted from pulmonary oedema (Bernstein *et al.*, 1961).

Several authors recommended 5 ml/kg of contrast agent for newborns (Henderson and Torch, 1977; Standen *et al.*, 1965). However, in view of our case of a newborn developing frank congestive failure and pulmonary oedema from slightly less than 5 ml/kg we recommend that the dose be no greater than 4 ml/kg. Since another neonate developed pulmonary oedema with 3.3 ml/kg perhaps the figure should be less than 3 ml/kg. Higher doses should be injected slowly. There should be valid indications for intravenous urography in small infants, especially those under 2 kg, because of thermal instability and the rapid changes in serum osmolarity. There are no good prospective studies on optimal intravenous urography dosage in neonates. The current recommendations are empirical. Investigations performed on adults and experimental animals suggest that dosages greater than 2 ml/kg for the usual contrast agents (Conray 60, Hypaque 50, Renografin 60) do not improve urography (McClennan *et al.*, 1971). However, this may not be valid for neonates.

REFERENCES

Ansell, G., 1970. Fatal overdose of contrast medium in infants. *British Journal of Radiology*, *43*, 395–396.

1976. *Complications in Diagnostic Radiology*, p. 22 (Blackwell Scientific Publications, Oxford).

Bernstein, E. F., Palmer, J. D., Aaberg, T. A., and Davis, R. L., 1961. Studies of the toxicity of Hypaque-90%, following rapid intravenous injection. *Radiology*, *76*, 88–95.

Busfield, D., Child, K. J., and Tomich, E. G., 1962. Pharmacological and toxicological studies on Triosil, an intravenous contrast agent. *British Journal of Radiology*, *35*, 815–823.

Henderson, K. C., and Torch, E. M., 1977. Differential diagnosis of abdominal masses in the neonate. *Pediatric Clinics of North America*, *24*, 557–578.

Hoppe, J. O., 1959. Some pharmacological aspects of radiopaque compounds. *Annals of the New York Academy of Sciences*, *78*, 727–739.

Kaufman, H. J., Probst, H., Breitenstein, R., and Oberholtzer, R., 1966. The testing of the LD_{50} for angiographic contrast media in the neonatal rat. *Annals de Radiologie*, *9*, 311–316.

Lachlan, H., 1970. Biochemical and other changes occurring in infants during angiocardiography. *Proceedings of the Royal Society of Medicine*, *63*, 46–48.

Lindgren, P., Saltzman, G.-F., and Tornell, G., 1968. Vascular reaction of water-soluble contrast media. *Acta Radiologica, Diagnosis*, *7*, 152–160.

McClennan, B. L., Becker, J. A., and Bredon, W. E., 1971. Excretory urography. Choice of contrast material—experimental. *Radiology*, *100*, 585–590.

McClennan, B. L., Kassner, E. G., and Becker, J. S., 1972. Overdose at excretory urography: toxic cause of death. *Radiology*, *105*, 383–386.

Malins, A. F., 1978. Pulmonary oedema after radiologic investigations of peripheral occlusive vascular disease adverse reaction to contrast media. *Lancet*, *1*, 413–415.

Mudd, J. G., Aykent, Y., and DeSchrijver, C., 1965. Hemodynamic, pathologic and cinegraphic effects of contrast media on the pulmonary vasculature. *Diseases of the Chest*, *48*, 55–63.

Salvesen, S., 1973. Acute toxicity tests of metrizamide. *Acta Radiologica; Supplement*, 335, 5–13.

Shehadi, W. H., 1975. Adverse reactions to intravascularly administered contrast media. *Americal Journal of Roentgenology*, *124*, 145–152.

Sotots, J. F., Dodge, P. R., and Talbot, N. B., 1962. Studies in experimental hypertonicity II. Hypertonicity of body fluids as a cause of acidosis. *Pediatrics*, *30*, 180–193.

Standen, J. R., Nogrady, M. B., Dunbar, J. S., and Goldbloom, R. B., 1965. The osmotic effects of methylglucamine diatrizoate (Renografin 60) in intravenous urography in infants. *American Journal of Roentgenology*, *93*, 473–479.

1979, *British Journal of Radiology*, *52*, 412–414

Case reports

Castleman's disease. Angiofollicular benign lymph-node hyperplasia. Radiological features in the differential diagnosis of vascular tumours of the pelvis

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In 1954 Castleman first described a thymoma-like mass in the anterior mediastinum (Castleman, 1954; Castleman *et al.*, 1956). The histology was that of a benign lymph-node hyperplasia. Many reports of this condition have since appeared in the literature (Abell, 1968; Anagnostou and Harrison, 1972; Blomquist, 1963). Descriptions in the radiological literature have been confined to thoracic lesions, presenting as asymptomatic well-defined homogenous masses involving lungs, lymph-nodes and mediastinum. These have been indistinguishable from other space occupying conditions such as thymoma, hamartoma, bronchial adenoma lymphoma and neurogenic tumours (Katz and Dziadiw, 1960; Wolfel *et al.*, 1964), the diagnosis being made by the pathologist. Although benign lymph-node hyperplasia (BLH) is most commonly found in the mediastinum, other sites in decreasing order of frequency are the lung hila, lungs, neck, axilla, retroperitoneum and pelvis (Keller *et al.*, 1972). Recently a patient was referred to us for angiography with a mass in the right pelvic cavity. Histologically the lesion was compatible with BLH.

As far as we can ascertain there has been no report of the radiological features of this condition within the pelvis. The purpose of this article is therefore to present the angiographic appearance of BLH which should be considered in the differential diagnosis of vascular tumours in the pelvis.

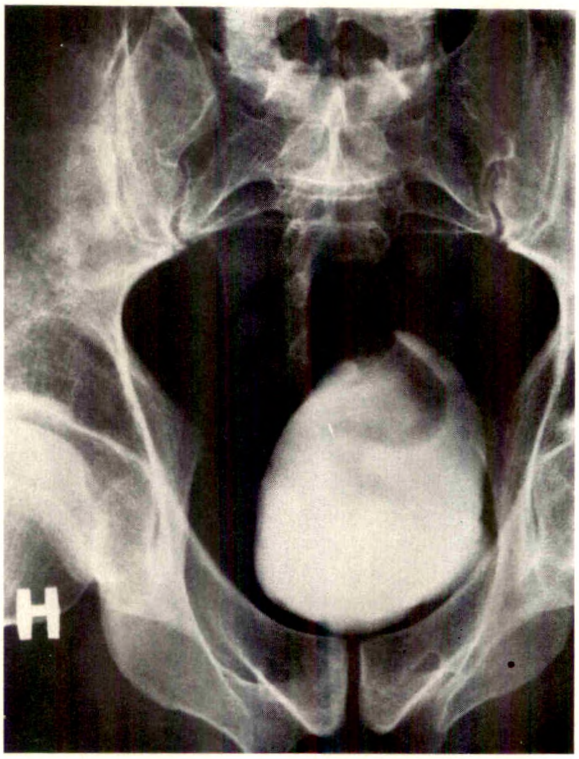

FIG. 1.

Excretion urogram showing compression and displacement of the bladder to the left.

CASE REPORT

A 58 year old caucasian male was referred to the National Hospital Reykjavik, giving a three year history of progressive swelling of his right thigh together with bouts of pain in the right groin radiating down the front of his thigh. During the last three to four months there was increasing weakness and tiredness preventing him from working as a telephone operator. Out patient investigation revealed an abnormal electrophoretic pattern in his serum proteins.

Past medical history: asthma of many years' duration, chronic sinusitis and recurrent exophthalmos due to retrobulbar hyperplasia necessitating five decompressive operations.

Clinical examination: the right thigh was 5 cm thicker than the left. A lump was palpable in the right groin and there was tenderness in the right iliac fossa but no obvious mass. Other signs elicited: exophthalmos with ptosis on the right and high pitched scattered rhonchi in both lung fields on forced expiration. The liver, spleen and lymph-nodes were not enlarged. On rectal examination there was fullness to the right.

Laboratory findings: Hb 14.0-13.1 gm, MCHC 31-33, ESR ranged between 37 and 45 mm/hr (Westergren), WBC 11000/ cc, serum proteins 7.5 g%, electrophoretic pattern Alb 36.6%, alpha-1 4, alpha-2 7.2%, gamma globulin 46.5% (normal level about 25%) IgG 5575 mg/100 ml (normal level 1000).

Liver function tests, urine analysis, bone marrow and chest X-rays were normal. Skeletal survey was normal apart from some osteoarthrosis of the lumbar spine. There was marked maxillary sinusitis.

Excretion urography showed moderate displacement of the right ureter towards the mid-line and an impression on the right wall of the bladder suggesting a mass (Fig. 1). This was substantiated by cystoscopy which revealed an intact mucosa with an extravesical space occupying lesion impinging on the right posterior aspect of the bladder.

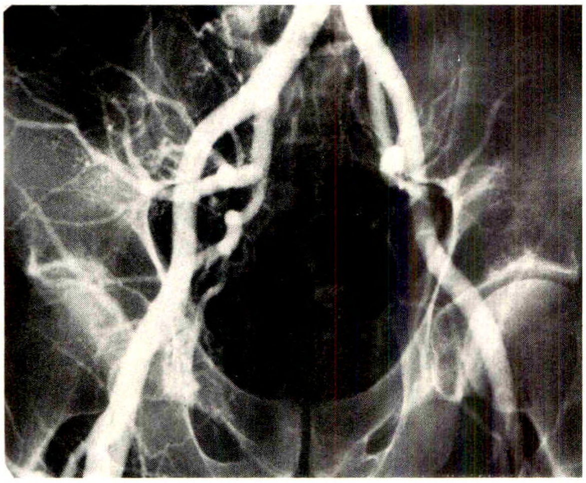

FIG. 2A.

Flush aortogram. There is enlargement of the arteries on the right side as compared to those on the left.

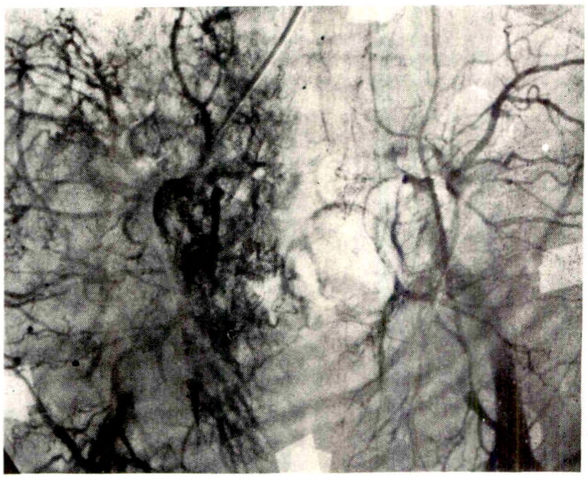

FIG. 2B.

Subtraction film. Midarterial phase: note the irregular vessels and premature filling of some veins.

Angiography of the pelvis was performed by the transfemoral route using the Seldinger technique (Seldinger, 1953). This revealed a highly vascular mass in the right pelvis extending from the mid-line to the iliac fossa and the inguinal ligament and ascending up to the level of the pelvic crest. The vascularity was uneven, the arteries being most numerous close to the mid-line near the bladder where the vessels were irregular and there was venous pooling. The mass was supplied mainly by branches of the right internal and external iliac arteries and to a lesser extent the lowermost right lumbar artery. The feeding vessels were considerably enlarged, especially the internal iliac artery and its branches (Fig. 2A). The transit time was prolonged, premature filling was present but no typical tumour vessels or contrast staining were seen (Figs. 2B, 2C). The inferior vena cava was displaced to the left (Fig. 3). Angiography suggested a benign retroperitoneal tumour or a chronic inflammatory process but gave no guide to the histology.

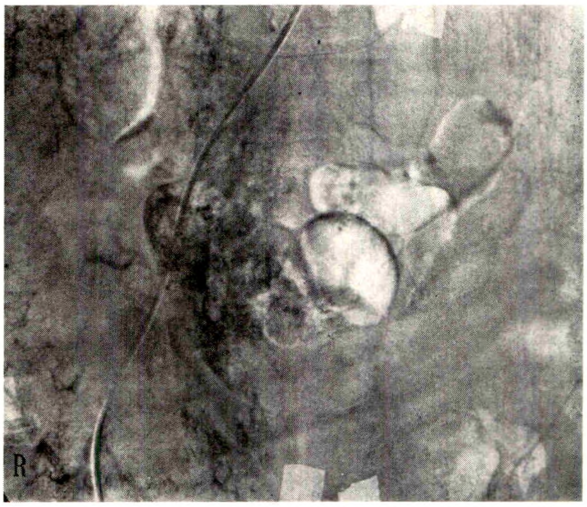

FIG. 2C.

Subtraction film, precapillary phase: innumerable tiny vessels scattered throughout the area. Pooling in veins. No neovascularity. Tumour blush was not seen.

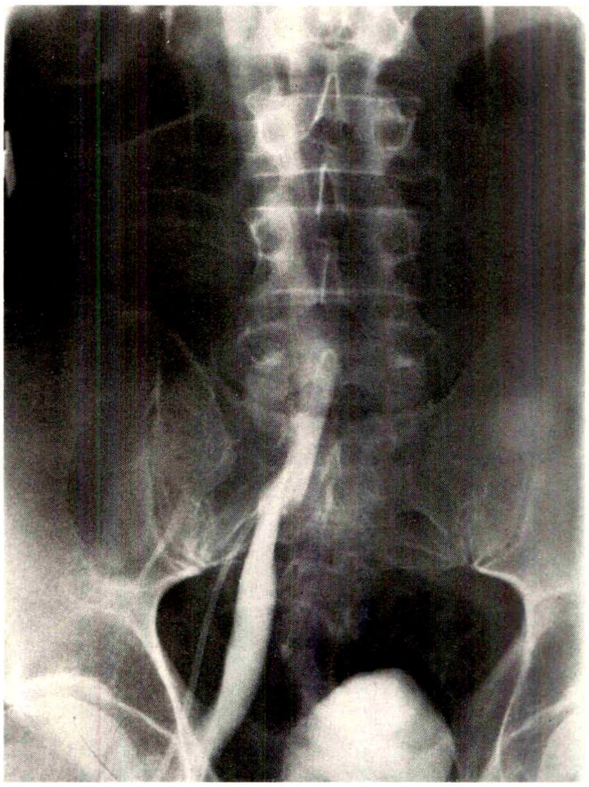

FIG. 3.

Cavogram showing displacement of the inferior vena cava to the left above the confluence of the common iliac veins.

Exploration revealed a firm, fibrous, vascular and fatty web-like mass studded with lymp-nodes and occupying most of the right pelvis. It extended from the femoral hiatus to well above the bifurcation of the aorta where a cord-like firm mass was felt retroperitoneally alongside the vertebrae. Piecemeal excision was carried out but it was impossible to remove the whole of the mass.

The histology was giant lymph-node hyperplasia (Castleman) of transitional type, including both plasma-cell and hyaline vascular lesions.

Discussion

The histology of BLH is well documented (Anagnostou and Harrison, 1972; Keller *et al.*, 1972). Microscopically about 90% show predominantly hyaline vascular changes and the remainder plasma-cell lesions. A combination of these features in the same lesion is distinctly uncommon. The hyaline vascular type is almost always symptomless apart from the result of pressure on adjacent structures. The plasma-cell lesions present with general systemic signs and symptoms including fever, anaemia, raised ESR leucocytosis and hypergammaglobulinaemia as reflected by the IgG fraction (Anagnostou and Harrison, 1972; Keller *et al.*, 1972. These manifestations remit with total removal of the lesion. The aetiology is unknown but most authorities suspect an infective agent or an immune reaction. Both sexes are equally affected and most patients are in the fourth or fifth decades. The lesions are non-invasive and do not metastasize to other parts of the body. Follow-ups of 15–20 years duration are recorded without evidence of recurrence (Griff and Griff, 1968).

Histologically our patient showed the rare transitional form with both plasma-cell and hyaline vascular changes. Clinically he illustrates the classic systemic changes found in the plasma-cell forms. Postoperatively the WBC returned to normal levels, the ESR remained at 40 mm/hr and the IgG fell from 5575 to 3359 mm/100 ml. The two latter readings are still raised and are probably due to incomplete removal of tumour tissue. Despite this the thigh diameter has diminished 3 cm. The patient has improved clinically, has no complaints and works full time.

Summary

An unusual case of benign lymph-node hyperplasia (Castleman) in the pelvis is reported and its clinical, histological and radiographic characteristics discussed. The angiographic appearances in this situation have to our knowledge not been described before in the literature. The angiographic features are not diagnostic, being mimicked by a wide variety of vascular tumours in the pelvis. The benign nature of the condition is stressed. BLH should be considered in the differential diagnosis of vascular tumours in the pelvis.

REFERENCES

Abell, M. R., 1968. Lymphnodal hamartoma. *Radiological Clinics of North America*, *6*, 15–24.

Anagnostou, Dimitra and Harrison, C. V., 1972. Angiofollicular lymph-node hyperplasia (Castleman). *Journal of Clinical Pathology*, *25*, 306–311.

Blomquist, H. E., 1963. Hyperplastic mediastinal lymph-nodes resembling thymoma. *Acta Chirurgica Scandinavica*, *126*, 66–77.

Castleman, B., 1954. Editor. Case records of the Massachusetts General Hospital. Case 40011. *New England Journal of Medicine*, *250*, 26–30.

Castleman, B., Iverson, L. and Menendez, V., 1956. Localized mediastinal lymph-node hyperplasia resembling thymoma. *Cancer*, *9*, 822–830.

Griff, L. C. and Griff, R. E., 1968. Mediastinal lymph-node hyperplasia. *British Journal of Radiology*, *40*, 68–69.

Katz, I. and Dziadiw, R., 1960. Localized mediastinal lymph-node hyperplasia. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *84*, 206–212.

Keller, A. R., Hochholzer, L. and Castleman, B., 1972. Hyaline-vascular and plasma-cell types of giant lymph-node hyperplasia of the mediastinum and other locations. *Cancer*, *29*, 670–683.

Seldinger, S. I., 1953. Catheter replacement of needle in percutaneous arteriography: new technique. *Acta Radiologica*, *39*, 368–376.

Wolfel, D. A., Antonius, J. I. and Cowley, R. A., 1964. Posterior mediastinal lymph-node hyperplasia. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *91*, 120–124.

Book review

An Atlas of Radiological Anatomy. By Jamie Weir and Peter Abrahams, pp. 287, illus., 1978 (Pitman Medical, Kent), £15·00.

This is an excellent 287 page atlas of radiographs and line drawings covering basic radiological anatomy. It is well presented although I feel that the quality of some of the radiographic plates could be improved. There has been a definite gap in the radiological literature and this book has gone a long way in filling it. However, in some respects there is insufficient detail for radiologists. If the balance of medical education were better all medical practitioners would be expected to know all these basic radiographic anatomical facts prior to qualification.

However, it is an excellent text to be recommended to all medical students, radiographers, physiotherapists, nurses and is essential for 1st year trainee radiologists.

A. B. Ayers.

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MAY 1979

Short communications

Hyperthermia and the oxygen enhancement ratio for damage to baby rat cartilage

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(*Received August, 1978 and in revised form December, 1978*)

One factor which may limit the sterilization of some tumours by radiotherapy is the presence of hypoxic cells which are resistant to treatment with X rays. Techniques to overcome this problem include the use of high pressure oxygen, high LET radiations such as fast neutrons, and hypoxic cell sensitizers. There are reports that each of these methods is more effective than X rays alone (Henk and Smith, 1977; Catterall, 1977; Urtasun *et al.*, 1977).

Hyperthermia has also been suggested as a possible method of cancer therapy, given either alone or in combination with X rays or drugs. It is therefore important to understand how hyperthermia and X irradiation may affect hypoxic cells. When hyperthermia has been combined with X rays there are indications that the oxygen enhancement ratio (OER) for cells *in vitro* has been reduced (Robinson *et al.*, 1974; Kim *et al.*, 1975a; Sutherland and Durand (in Bronk), 1976). Dewey *et al.* (1977) called this "... one of the most important aspects of hyperthermia which may indeed be the source of the poor man's high LET radiation". There are also several reports that hypoxic cells *in vitro* are just as sensitive to direct heat damage as are well oxygenated cells (Kim *et al.*, 1975b; Harisiadis *et al.*, 1975). Studies *in vivo* have shown that clamping the blood supply to a limb or organ causes a dramatic sensitization of tissue to direct heat damage. This is true both for tumours and normal tissues (Suit, 1977; Hill and Denekamp, 1978; Morris *et al.*, 1977). However, there is evidence from experiments with cells *in vitro* that low pH or nutrient deficiency also cause a dramatic increase in cell sensitivity to direct heat damage (Overgaard 1976; Gerweck and Rottinger, 1976; Hahn, 1974). The problems of separating the effects of hypoxia, low pH and nutritional deprivation *in vivo* make it difficult at present to understand which are the critical factors involved in the increased sensitivity.

In addition, with cells *in vitro* it is difficult to determine whether cells die from direct heat damage or from heat-enhanced X-ray damage. For direct heat damage such a separation between the two responses can be made with experiments *in vivo* because the effects may differ qualitatively, or in the time course of their development (*e.g.* Law *et al.*, 1978; Morris *et al.*, 1977; Myers and Field, 1977).

METHOD

In the present study, cartilage in the tails of baby rats was used to examine the response of a normal tissue *in situ* to combined heat and X irradiation under both normal and hypoxic conditions. Whereas direct heat damage to the tail causes necrosis (Morris *et al.*, 1977), X rays alone or X rays enhanced by hyperthermia cause a stunting of vertebral growth (Myers and Field, 1977). Only the distal half of the tail was treated. The mean length of a group of vertebrae in the treated portion was compared with normal growth in the untreated portion and a percentage stunting obtained for each rat. To induce hypoxia the blood supply to the tail was occluded using a thin rubber cuff. In these experiments, the cuff was applied only 3–4 minutes prior to and during X irradiation. For hyperthermia, tails were heated to 43°C for one hour and X irradiation was begun five minutes after the end of the heating. Radiographs of the tails were taken 13 weeks later and the lengths of the treated vertebrae were measured. The results are shown in Figs. 1 and 2. The heat treatment (43°C for one hour) given alone caused no observable damage.

RESULTS

The curves shown in Figs. 1 and 2 were fitted by regression analysis. The intercepts obtained by this initial analysis were found to be different from one another, but not significantly so. A weighted mean of these was calculated and included as a point for recalculation of the curves. The OER values thus obtained from the slope ratios were 2.03 for X rays alone and 2.28 when the tails were pre-treated. These were shown to be not significantly different from one another and thus there was no indication of a reduction in OER by hyperthermia.

Thermal enhancement ratios (TERs) were also calculated as slope ratios and found to be 1.68 for clamped conditions and 1.88 for normal conditions. Previously we have shown that the TER is dependent on the level of damage at which it is assessed (Myers and Field, 1977). However, in this study, where regression lines have been fitted to the data, no such dependence is seen.

DISCUSSION

Radiobiological hypoxia as induced in most *in vitro* test systems may be accompanied in many cases by nutrient deficiency and low pH in the cell medium. Although the work by Robinson *et al.* (1974) and Kim *et al.* (1975a) suggested that oxygen depletion was responsible for the increased radiosensitization of "hypoxic" cells by heat (*i.e.* reduction in OER), there was no mention of control of

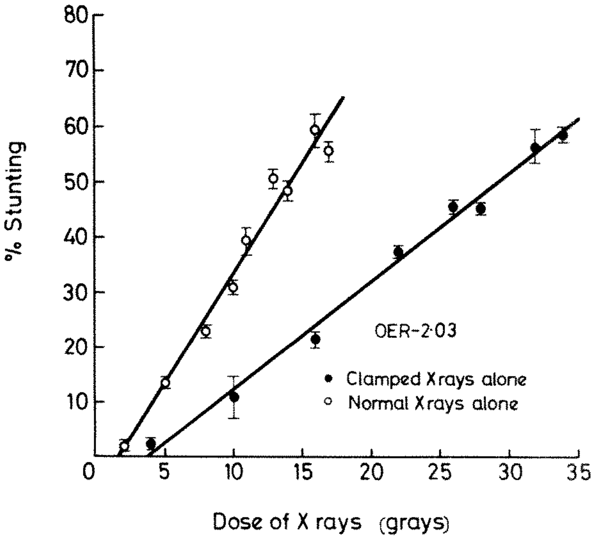

Fig. 1.

Dose-effect curves for X rays alone to normal and clamped baby rat tails, showing percentage stunting *vs.* dose of X rays The slopes of the regression lines give an OER of 2.03.

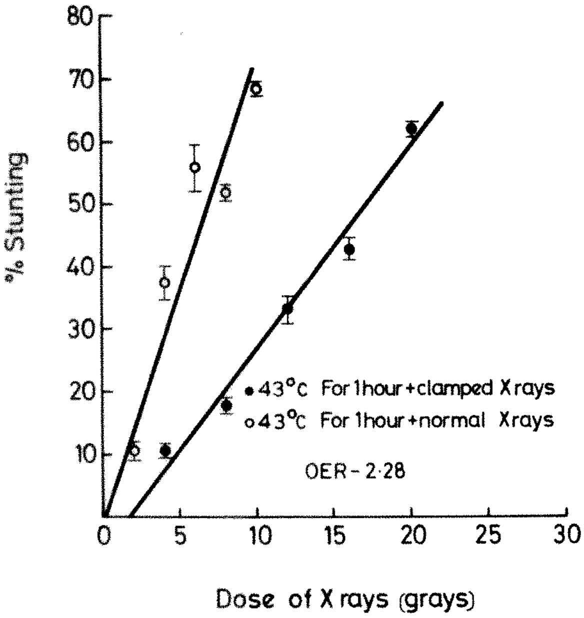

Fig. 2.

Dose-effect curves for X rays to normal and clamped baby rat tails after a heat treatment of 43°C for 1 hour. The slopes of the regression lines give an OER of 2.28. The vertical lines show standard errors.

nutrient levels or pH in the report by Kim *et al.* (1975a) although Robinson has stated that the pH in his system was measured and found to be constant (personal communication). The probability of undetected direct cell killing by hyperthermia would increase if the pH was reduced and and could certainly lead to the measured reduction of OER in the above experiments. Power and Harris (1977) using normal and tumour cells *in vitro* achieved extreme hypoxia by passive gas exchange rather than by respiration-assisted oxygen depletion. They claimed that their cells experienced no nutritional stress or variation of pH. They observed no change in OER at 43°C and suggested that neither hypoxia, pH nor nutrient deficiency could alone be responsible for the increased sensitivity of hypoxic cells at elevated temperatures. Kiefer *et al.* (1976) also observed no decrease in OER in diploid yeast cells heated at 47°C.

It seems therefore that there are discrepancies in the *in vitro* results which have been reported with a clear demonstration that different experimental techniques can lead to different conclusions. Data presented by Thrall *et al.* (1975) from work carried out on mouse foot skin also indicate no decrease in OER after pre-heating. By clamping the blood supply of the rat tail we have made the tissue "radiobiologically hypoxic" giving an OER of about 2·0. This OER value is similar to that found by Dixon (1967) who previously found an OER of 2·3 using this system. It is probable that the trend towards a higher OER value after heating is due to better oxygenation due to increased blood flow in the unclamped tails. Whether or not clamping causes other physiological changes and whether they are similar to conditions in poorly vascularized tumours is not known, but we have found no decrease in OER of the tissue for combined heat and radiation, which does not support the view that hyperthermia may be a substitute for high LET radiation in this respect.

In conclusion, hyperthermia may selectively kill hypoxic cells. However, these experiments demonstrate that heating to levels which are insufficient to cause any observable cell killing does not result in a differential sensitization of hypoxic cells to subsequent X irradiation.

REFERENCES

Bronk, B. V., 1976. Thermal potentiation of mammalian cell killing: clues for understanding and potential for tumour therapy. *Advances in Radiation Biology*, *6*, 267–324.

Catterall, M., 1977. The treatment of cancer of the head and neck: fast neutrons—the way ahead? *Seminars in Oncology*, *4*, 407–411.

Dewey, W. C., Hopwood, L. E., Sapareto, S. A. and Gerweck, L. E., 1977. Cellular responses to combinations of hyperthermia and radiation. *Radiology*, *123*, 463–474.

Dixon, B., 1967. The effect of radiation on the growth of vertebrae in the tails of rats. I. Single doses of X rays and the effect of oxygen. *International Journal of Radiation Biology*, *13*, 355–368.

Gerweck, L. E. and Rottinger, E., 1976. Enhancement of mammalian cell sensitivity to hyperthermia by pH alteration. *Radiation Research*, *67*, 508–511.

Hahn, G. M., 1974. Metabolic aspects of the role of hyperthermia in mammalian cell inactivation and their possible relevance to cancer treatment. *Cancer*, *34*, 3117–3123.

Harisiadis, L., Hall, E. J., Kraljevic, U. and Borek, C., 1975. Hyperthermia: biological studies at the cellular level. *Radiology*, 117. 447–452.

Henk, J. M. and Smith, C. W., 1977. Radiotherapy and hyperbaric oxygen in head and neck cancer. *The Lancet*, *2*, 104–105.

Hill, S. A. and Denekamp, J., 1978. The effect of vascular occlusion on the thermal sensitization of a mouse tumour. *British Journal of Radiology*, *51*, 997–1002.

Kiefer, J., Kraft-Weyrather, W, and Hlawica, M. M., 1976. Cellular radiation effects and hyperthermia: influence of exposure temperature on survival of diploid yeast irradiated under oxygenated and hypoxic conditions. *International Journal of Radiation Biology*, 30, 293–300.

Kim, S. H., Kim, J. H. and Hahn, E. W., 1975a. The radiosensitization of hypoxic tumour cells by hyperthermia. *Radiology*, *114*, 727–728.

1975b. Enhanced killing of hypoxic tumour cells by hyperthermia. *British Journal of Radiology*, *48*, 872–874.

Law, M. P., Ahier, R. G., and Field, S. B., 1978. The response of the mouse ear to heat applied alone or combined with X rays. *British Journal of Radiology*, *51*, 132–138.

Morris, C. C., Myers, R. and Field, S. B., 1977. The response of the rat tail to hyperthermia. *British Journal of Radiology*, *50*, 576–580.

Myers, R. and Field, S. B., 1977. The response of the rat tail to combined heat and X rays. *British Journal of Radiology*, *50*, 581–586.

Overgaard, J., 1976. Influence of extracellular pH on the viability and morphology of tumour cells exposed to hyperthermia. *Journal of the National Cancer Institute*, *56*, 1243–1250.

Power, J. A. and Harris, J. W., 1977. Response of extremely hypoxic cells to hyperthermia: survival and oxygen enhancement ratios. *Radiology*, *123*, 767–770.

Robinson, J. E., Wizenberg, M. J. and McCready, W. A., 1974. Combined hyperthermia and radiation suggest an alternative to heavy particle therapy for reduced oxygen enhancement ratios. *Nature*, *251*, 521–522.

Suit, H. D., 1977. Hyperthermic effects on animal tissues. *Radiology*, *123*, 483–487.

Thrall, D. E., Gillette, E. L. and Dewey, W. C., 1975. Effect of heat and ionising radiation on normal and neoplastic tissue of the C3H mouse. *Radiation Research*, 63, 363–377.

Urtasun, R. C., Miller, J. D. R., Frunchak, V., Koziol, D., Band, P. R., Chapman, J. D. and Fieldstein, M. L., 1977. Radiotherapy pilot trials with sensitisers of hypoxic cells. Metronidazole in supratentorial glioblastomas. *British Journal of Radiology*, 50, 602–603.

1979, *British Journal of Radiology*, *52*, 417–418 MAY 1979

Short communications

Optimal fractionation for the radiotherapy of tumour cells possessing wide-shouldered survival curves

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Though the radiocurability of human tumours varies widely, most cells in culture prove to have rather similar radiation survival curves. A small number of tumours, however, including melanoma (Dewey 1971; Barranco *et al.*, 1971), osteosarcoma (van Putten 1968) and rhabdomyosarcoma (Rheinhold 1966), have been reported to possess unusually wide-shouldered survival curves for cells growing in culture.

These observations have given rise to the suggestion that there may exist a sub-class of radioresistant tumours whose resistance is due to a wide-shoulder rather than to a shallow terminal slope of the survival curve. Such tumours might be treated more effectively by a small number of large-dose fractions of radiation, than by a conventional schedule (Hornsey 1972; Wheldon and Kirk 1975). This contention is supported by the results of a recent clinical trial (Habermalz and Fischer 1976) and retrospective survey (Hornsey 1978) in the case of malignant melanoma, and by very preliminary clinical indications in the case of osteogenic sarcoma (Goffinet *et al.*, 1975; Kaplan 1977).

Very recently, Zeitz and McDonald (1978) have drawn attention to the large numerical differences obtained for the prediction of cell survival following fractionated irradiation, according to the mathematical model chosen to represent the cell survival curve. These authors considered four treatment schedules presumed to have equivalent effects on normal connective tissue. They computed cell survival probability using three mathematical models fitted to the *in vitro* data of Dewey (1971) on melanoma cells and demonstrated that, at least for small fraction sizes, the numerical results were heavily dependent on choice of model.

Zeitz and McDonald (1978) are clearly right to emphasize the existence and magnitude of these differences, but their conclusion that the resultant uncertainties "could be so large as to make estimates (of cell survival) of little or no value" is excessively severe. This is demonstrated in Table I.

As may be seen, the predicted order of superiority of the four schedules is the same for all three models, though the absolute value of the differential, in terms of cell survival, between the best schedule (IV) and the worst schedule (I) ranges between six and eleven factors of ten according to model chosen. The appropriate conclusion would seem to be that the data of Dewey (1971) unequivocally point to the superiority of large doses per fraction, though the absolute magnitude of this superiority depends on the model used.

Other objections may be put, however. As Zeitz and McDonald (1978) also note, there exists no consensus regarding the shape of the survival curve for melanoma cells. Table II summarizes the findings of several authors, using D_Q as a measure of shoulder width, and shows that five out of seven studies *in vitro* indicated a shoulder width in excess of 200 rad, while the one *in vivo* study gave a small extrapolation number with a shallow terminal slope suggestive of a hypoxic survival curve. Despite these variations, the tendency to observe a wider than average shoulder width for the survival curve of melanoma cells is apparent.

All the preceding calculations were based on survival curves for well-oxygenated cells which were therefore presumed to be the dominant cell type governing radiocurability. The importance of hypoxic cells is well-established in the case of experimental tumours, and the same can be presumed in human tumours. There is general agreement that the slope of the terminal exponential portion of cell survival

TABLE I

IMPLICATIONS OF THE ANALYSIS OF ZEITZ AND MCDONALD (1978) FOR CHOICE OF TREATMENT SCHEDULES (DATA OF DEWEY, 1971)

Model	Schedules in order of superiority	Differential advantage of best over worst schedule
Simple multitarget $n = 15$ $D_0 = 94$ rad	IV, III, II, I	1.18×10^{-11}
Linear-quadratic $\alpha = 7.4 \times 10^{-4}$ rad^{-1} $\beta = 8.4 \times 10^{-6}$ rad^{-2}	IV, III, II, I	4.0×10^{-11}
Multitarget with non-zero initial slope $D_1 = 327$ rad $D_0 = 108$ rad $n = 53$	IV, III, II, I	1.23×10^{-6}

Note: Schedules are defined as follows:
I: 31 × 200 rad; II: 7 × 620 rad
III: 4 × 960 rad; IV: 3 × 1200 rad

These schedules are presumed equivalent for normal tissues as assessed by the NSD formula.

TABLE II

SUMMARY OF EXPERIMENTAL FINDINGS ON THE SHOULDER WIDTH OF THE SURVIVAL CURVE FOR MALIGNANT MELANOMA CELLS.

Authors	Species	Radiation Conditions	D_Q rad
Dewey (1971)	Mouse	*in vitro*	254
Barranco *et al.*, (1971)	Man	*in vitro*	314
Thomson *et al.*, (1975)	Man	*in vitro*	329
Zeitz & Sigali (1977)	Mouse	*in vitro*	94
Guichard *et al.*, (1977)	Man	*in vitro*	230
Guichard *et al.*, (1977)	Man	*in vivo*, as xenograft	158
Smith *et al.*, (1978)	Man	*in vitro*	216
Weininger *et al.*, (1978)	Man	*in vitro*	183

D_Q is the intercept on the abcissa of the extrapolated exponential portion of the survival curve and constitutes a measure of shoulder width. A typical value of D_Q for a well-oxygenated cell line ($n = 2$, $D_0 = 130$ rad) would be about 90 rad. Less than 20% of all cell lines have D_Q in excess of 200 rad (Hornsey 1972). Where more than one cell line was studied, the D_Q value cited in the table is derived from the parameters cited as representative by the authors, or is the arithmetic average of the D_Q values for each line.

curves is reduced, typically by a factor of between two and three. No such consensus exists however, regarding the effect of hypoxia on the early, shouldered part of the survival curve, but there is some evidence that hypoxia may abolish or reduce the width of the shoulder (Revesz *et al.*, 1975; Guichard *et al.*, 1977). Whether this phenomenon is a general one is not yet known.

I have computed the theoretical cell survival probabilities for each of the four schedules considered by Zeitz and McDonald (1978) for two hypothetical survival curves for anoxic melanoma cells. These curves are obtained from data of Dewey (1971) on the survival curve of oxygenated cells, using the multi-target model with non-zero initial slope (found by Zeitz and McDonald to provide the best fit to these data) and transforming the model parameters by assuming a dose-modifying factor of 2.5 and either (a) shoulder unchanged, or (b) shoulder abolished.

The results, presented in Table III, show that the advantage now passes to schedule I whether the shoulder is retained or abolished. No allowance has been made in these calculations for either re-population or re-oxygenation, though the former effect is unlikely to alter the order of superiority of the schedules if each is administered in the same overall time.

Re-oxygenation, however, which is highly variable between different experimental tumours, could be of critical importance in determining whether oxic or hypoxic cells are the more important at any moment. If re-oxygenation is brisk during therapy, oxic cells continue to control the surviving fraction and schedule IV should, again, be used throughout. If, however, re-oxygenation takes place slowly or not at all during therapy, hypoxic cells become increasingly important as treatment proceeds. This suggests a non-uniform schedule in which large doses per fraction (as in schedule IV) gradually give way to smaller doses per fraction (as in schedule I). It would seem therefore that large doses per fraction should logically be used at least in the early stages of therapy and perhaps throughout.

TABLE III

Predicted survival probabilities for anoxic melanoma cells treated with alternative schedules

Form of survival curve	Model parameters	Probability of cell survival for schedules			
		I	II	III	IV
Shoulder Fully Retained	$D_1 = 818$ rad $D_0 = 270$ rad $n = 53$	5.11×10^{-4}	4.84×10^{-3}	3.47×10^{-3}	1.24×10^{-3}
Shoulder Completely Abolished	$D_1 = \infty$ $D_0 = 270$ rad $n = 1$	1.0×10^{-10}	1.05×10^{-7}	6.66×10^{-7}	1.6×10^{-6}

Schedules are defined as for Table I. The model is the multitarget model with non-zero initial slope. The parameters are obtained by transforming those of Zeitz and McDonald (1978) for the data of Dewey (1971) by assuming a dose-modifying factor of 2.5 and either (a) full retention of shoulder or (b) complete abolition of shoulder. No allowance is made for repopulation or reoxygenation.

While it is no doubt premature to draw firm conclusions on the basis of the data presently available, these considerations continue to provide encouragement that there may exist a class of radioresistant tumours whose response to treatment might be substantially improved by a more appropriate choice of treatment schedule. Further work to identify such tumours, and to characterize their oxic and hypoxic survival curves *in vitro* and *in vivo* seems warranted.

REFERENCES

Barranco, S. C., Romsdahl, M. M. and Humphrey, R. M., 1971. The radiation response of human malignant melanoma cells grown *in vitro*. *Cancer Research*, *31*, 830–833.

Dewey, D. L., 1971. The radiosensitivity of malignant melanoma cells in culture. *British Journal of Radiology*, *44*, 816–817.

Goffinet, D. R., Kaplan, H. S., Donaldson, S. S., Bagshaw, M. A. and Wilbur, J. R., 1975. Combined radiosensitizer infusion and irradiation of osteogenic sarcoma. *Radiology*, *117*, 155–158.

Guichard, M., Gosse, C. and Malaise, E. P., 1977. Survival curve of human melanoma cells in nude mice. *Journal of the National Cancer Institute*, *58*, 1665–1669.

Habermalz, H. J. and Fischer, J. J., 1976. Radiation therapy of malignant melanoma. *Cancer*, *38*, 2258–2262.

Hornsey, S., 1972. The radiosensitivity of melanoma cells in culture. *British Journal of Radiology*, *45*, 158.

Hornsey, S., 1978. The relationship between total dose, number of fractions, and fraction size in the response of malignant melanoma in patients. *British Journal of Radiology*, *51*, 905–909.

Kaplan, H. S., 1977. Fundamental mechanisms in combined modality therapy of cancer. *American Journal of Roentgenology*, *129*, 383–389.

Revesz, L., Littbrand, B., Midlander, J. and Scott, O. C. A., 1975. Oxygen effects in the shoulder region of cell survival curves. In *Cell Survival after Low Doses of Radiation* (T. Alper, Ed.) Institute of Physics and John Wiley, London.

Rheinhold, H. S., 1966. Quantitative evaluation of the radiosensitivity of a transplantable rhabdymyosarcoma of the rat. *European Journal of Cancer*, *2*, 23–42.

Smith, I. E., Courtenay, V. D., Mills, J. and Peckham, M. J., 1978. *In vitro* radiation response of cells from four human tumours propagated in immune-suppressed mice. *Cancer Research*, *38*, 390–392.

Thomson, L. F., Smith, A. R. and Humphrey, R. M., 1975. The response of a human melanoma line to high LET radiation. *Radiology*, *117*, 155–158.

Van Putten, L. M., 1968. Tumour oxygenation during fractionated radiotherapy: studies with a transplantable mouse osteosarcoma. *European Journal of Cancer*, *4*, 173–182

Weininger, J., Guichard, M., Joly, A. M., Malaise, E. P. and Lachet, B., 1978. Radiosensitivity and growth parameters *in vitro* of three human melanoma strains. *International Journal of Radiation Biology*, *34*, 285–290.

Wheldon, T. E. and Kirk, J., 1975. Optimal radiotherapy of radioresistant tumours. *British Journal of Radiology*, *48*, 870–871.

Zeitz, L. and Sigali, S., 1977. Radiosensitivity of melanoma cells in culture: implications for the radiotherapy of malignant melanoma. *British Journal of Radiology*, *50*, 604–608.

Zeitz, L. and McDonald, J. M., 1978. Pitfalls in the use of *in vitro* survival curves for the determination of tumour cell survival with fractionated doses. *British Journal of Radiology*, *51*, 637–639.

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Short communications

The provision of a district nuclear medicine service

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The high cost of nuclear medicine equipment, together with the necessary radiopharmaceutical facilities, has led to the establishment of departments of nuclear medicine mainly in the major hospital of a district or area. This necessitates the transport of patients from other hospitals to the department by ambulance, usually accompanied by an escort nurse. Certain categories of patient are unable to travel and are not studied. Ambulance transport can lead to timing problems—if an ambulance is late in arriving, the department's schedule can be thrown into chaos while, if the return journey is delayed, patients may spend long periods in the often unsuitable and cramped waiting area.

Following the introduction of mobile cameras, an alternative procedure is to take the service to the patients by transporting a camera to the other hospitals in a group together with any necessary radiopharmaceuticals and equipment. A pilot study has been carried out, providing a service on one day per week to another hospital in our district.

The camera (Searle LEM) was delivered to the site on the evening preceding use together with a dose calibrator, radiation monitor, gloves, needles etc: three people, including the driver, were found adequate for the task of loading and unloading. No special precautions to safeguard the detector were taken other than to leave the collimator fitted: the truck was not equipped with air-conditioning. The average duration of the journey was between 30 minutes and one hour.

At the daughter hospital, an empty room was needed at least 4 metres square with a door wide enough for a patient's trolley to pass through and containing at least two 13 amp sockets, one for the gamma camera and one for an ionization chamber. If X-ray film is used as the image recording medium, proximity to the X-ray department's processor is desirable while the location is immaterial if Polaroid film is used.

Requests for investigations were made to the base department in the normal way, and non-urgent studies were arranged for an appropriate day at the daughter hospital. Urgent requests, except for those made when the camera was at the daughter hospital, were dealt with as before, the patient being transported to the base department. Individual doses of radiopharmaceuticals were made up in the base department for each patient, appropriately packaged (*Code of Practice for the Carriage of Radioactive Materials by Road, HMSO*, 1975: for exemption limits see Health Notes HN (78) 37). Materials, accompanied by two members of staff, were taken to the daughter hospital on the routine mail transport vehicle and on arrival each dose was unpacked, checked in the dose calibrator and placed in a shielded container. Radiopharmaceuticals required for urgent investigations requested when the camera was at the daughter hospital were sent from the base department by van on the scheduled district mail runs. Radiopharmaceuticals were administered on the ward by a member of the referring firm, who was issued with a film badge dosimeter if not already a designated radiation worker.

A range of static studies including bone, brain, liver and lung were undertaken. The LEM gamma camera is capable also of producing a twelve-image dynamic study on one film and, together with the separate computer module, of performing gated cardiac studies, renography and other dynamic investigations. Thus, apart from the necessity of using a diverging collimator to view large organs, the full range of studies offered by the base department may be undertaken.

Images were returned to the base department at the end of the day for interpretation; verbal reports were telephoned to the appropriate wards, followed by written reports later. All waste was returned to the base department for disposal. After initial minor logistic difficulties, the scheme worked well and was received with enthusiasm by the medical and nursing staff of the daughter hospital.

While, in this pilot study, every attempt was made to provide a completely self-contained service, a more flexible and effective service could be provided if minimal radiopharmaceutical dispensing facilities were available at the daughter hospital. This would allow stock solutions of radionuclides and a selection of radiopharmaceutical kits to be transported, the doses being prepared on-site as required. In addition, if members of the local medical staff were trained in nuclear medicine, perhaps by temporary attachment to the base department, or alternatively if junior nuclear medicine staff travelled with the camera, immediate reports would be available to the referring clinician: such trained staff could also administer the radiopharmaceuticals.

Further development of this "sessional nuclear medicine" approach could either take the form described above or else that used, very successfully, for a whole-body counter (Boddy, 1967) in which the equipment is mounted in an air-conditioned van. The latter method would have the advantage that the gamma camera would not be subjected to such rough handling or to temperature changes but could be disadvantageous in terms of access to the vehicle and in the lack of space for adequate positioning of the patients.

Considering the costing involved, the LEM camera is valued at £48000 complete except for the computer trolley, which is a further £12000. Even if a truck is not already available and has to be purchased specifically for this purpose, the additional cost would be approximately £9000, giving a total capital cost of £69000. Running costs would be approximately £12000 per annum for a radiographer or technician, driver and servicing of camera and truck. Building costs are ignored since use can be made of a multipurpose room (such as a seminar room or out-patient clinic area) to house the camera during its visits.

In our case, such a mobile camera would be used to provide services to at least three hospitals on a routine basis and the comparative capital cost of three fixed installations would be in excess of £150000 for the cameras with an additional (notional) figure of £24000 to provide the necessary space and services in a new building, the latter figure being substantially less if existing accommodation was upgraded. Running costs, for camera servicing and staffing of one full-time and two part-time radiographers or technicians, would be approximately £14500 per annum.

It can be seen that the mobile camera offers substantial savings on capital investment and a modest advantage in running costs over the multiple fixed installations. In comparing the mobile system against the cost of a single fixed installation and transporting patients to the base department, the advantages of the mobile system cannot be quantified so readily. Nevertheless, the additional cost of the truck, its servicing and the provision of a driver (where necessary) can be set against a notional cost of £1 per mile for non-emergency ambulance services plus the cost of providing an escort nurse in certain cases. The less objective advantages, such as being able to offer a nuclear medicine service to a wider range of in-patients (and a local service for out-patients) at the daughter hospitals and of releasing ambulances and crews for more vital duties, must remain matters for individual evaluation.

It should be noted that, in choosing a mobile camera, weight is an important factor, since many hospital lifts in the UK have a maximum load capacity of 1000kg or under.

We believe that the operation of a mobile system offers a useful and cost-effective means of extending nuclear medicine services to a greater proportion of patients throughout a district or area.

ACKNOWLEDGMENT

The authors are grateful to G. D. Searle foi the loan of the mobile camera used.

REFERENCE

BODDY, K., 1967. A high sensitivity shadow-shield whole body monitor with scanning-bed and tilting chair geometries, incorporated in a mobile laboratory. *British Journal of Radiology*, *40*, 631–637.

Book review

A Study Guide for Radiologic Technologists. By Judith P. Baron, pp. 540, 1978 (Charles C. Thomas, Springfield, Illinois) $17.50.
ISBN 0–398–03726–4.

According to its cover this book is designed to complement classroom instruction in radiological physics, radiographic circuitry, basic radiographic accessories and radiation biology. Mrs. Baron has devised a new system to help readers to understand the basic physics and radiobiology from first principles and to organize isolated bits of knowledge into larger ideas. The book is divided up into numbered frames and each piece of information is put into one of these frames. The frames are presented in sequence, through which technical terms are defined and concepts developed. Interspersed with the frames are information panels, summaries and student evaluations, consisting of questions relating to the previous chapter. As the reader progresses through the book, there are constant opportunities to refer back and reinforce earlier concepts, made easy by the numbered frame system. I found the programme worked very well indeed. However, leaving a blank space in each frame, and printing the missing word in heavy type at the bottom left corner, is distracting, particularly when the missing word is not a key word.

Having grasped the system, the reader is launched into Chapter 1: basic information concerning matter, energy, and units of measurement. There are readily appreciated analogies to describe kinetic and potential energy. Having first been firmly told that the unit of weight is the kilogram, the reader finds that people's weight is still discussed in pounds! The atomic structure of matter, electrical properties and electron energy levels are all simply and clearly described. There is a reference list at the back of the book for those who wish to enlarge on this basic information. Chapter 2 follows logically with electrostatics, methods of electrification, descriptions of how electrons move and five laws of electrostatics. Chapters 3 and 4 deal with electrodynamics and electromagnetism, describing current, potential difference and capacitance. Fundamental matters such as the amp, EMF, resistance, and Ohm's Law are clearly defined. Solenoids and electromagnets are dealt with, and electromagnetic induction leads on to the next section which deals with alternating current generators and motors. Three phase generators and induction motors are well described, with examples of their use in X-ray equipment. A section on the production and control of voltage in radiographic circuits follows, including step-up and step-down transformers, transformer laws and current control by rheostats. The next two chapters concern rectification of alternating current, describing half- and full-wave rectification, valves, solid state rectifiers, photo electric tubes and their application as timers. X-ray tube design is also covered, including a description of a grid biased tube. The chapter on X-ray circuits is very basic and would need to be heavily supplemented by any student working for a D.C.R. equipment paper. The nature, production and properties of X rays come next, and this is full and informative. It is followed by a section dealing with image production. I found the description of latent images unnecessarily complicated, but the part dealing with films and screens was useful. Improving the image by the use of diaphragms, cones and grids is fully covered. There is an excellent section on radiation biology, the measurement of ionizing radiations and their effect on living tissue. I found the author's presentation easy to understand and fascinating. The reader learns how radiation (electromagnetic or particulate) interacts with matter, how biological molecules may be altered and how in the case of DNA the changed molecule may carry a new reproductive message, causing mutations. Cells which are radiosensitive are listed and advice on patient protection given. Finally, a brief résumé of advances in imaging modalities is given, mentioning image intensifiers, tomography, xeroradiography etc. I would have expected some mention of ultrasound here, but there was none.

This is a very long book, and full of information. Mrs. Baron indicates in her preface that her object is to give a good working knowledge of the production of X radiation and its properties, so that the radiographer may achieve a good quality, diagnostic film, with the least radiation dose to the patient and the greatest protection to the operator. I think she has succeeded. She has been badly served by her publisher, however. The list of contents at the beginning is correct as far as page 5. Thereafter, nothing appears on the page stated, and the index has been left out altogether. A comprehensive book such as this needs its index (which is listed in the contents), and it is hard to understand how the book was released with such a glaring fault. Despite this it would be a valuable addition to the shelves of any radiographic school library.

PAT HOLISTER.

1979, *British Journal of Radiology*, *52*, 421

MAY 1979

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Interface dosimetry

THE EDITOR—SIR,

In a recent letter Lowe (1978) claimed that the measurements of Dutreix *et al.* (1962) on the variation in ionization across a copper–carbon interface are misrepresented in later publications by Dutreix and Bernard (1966) and Spiers (1969).

The original measurements were of the ionization in an air-filled cavity at positions on either side of the interface and the results were initially presented graphically with the ratio of the observed ionization to that obtained for a carbon chamber of equilibrium wall thickness U(Cu/C) plotted as the ordinate.

It is indeed true that in the subsequent publications this axis was relabelled in terms of a dose ratio. The ratio is not however simply that of the absorbed dose to the medium at the position in question relative to the equilibrium dose in the lower atomic number medium, as Lowe seems to assume.

Dutreix and Bernard (1966) clearly state that "the dotted curve in the copper corresponds to the dose in an infinitely small mass of water located in the copper", while Spiers (1969) similarly notes that "the curves inside the Cu zone give the doses in a very small air (or tissue) volume within the copper".

If $D_{\mathrm{C,H_2O}}$ is the absorbed dose in the low atomic number component (carbon or water) at a point remote from the interface, where electronic equilibrium has been re-established, the corresponding dose in the copper D_{Cu} will, assuming negligible attenuation across the interface, be given by:

$$D_{\mathrm{Cu}}=\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{C,H_2O}}}\cdot D_{\mathrm{C,H_2O}}$$

where μ_{Cu} and $\mu_{\mathrm{C,H_2O}}$ are the mass energy absorption coefficients of the media involved. The doses to a small volume of medium Z contained within a cavity located in such regions will, however, be:

$${}_{\mathrm{C,H_2O}}D_Z=\frac{mS_Z}{mS_{\mathrm{C,H_2O}}}\cdot D_{\mathrm{C,H_2O}}$$

for a cavity in the low atomic number component and

$${}_{\mathrm{Cu}}D_Z=\frac{mS_Z}{mS_{\mathrm{Cu}}}\cdot D_{\mathrm{Cu}}=\frac{mS_Z}{mS_{\mathrm{Cu}}}\cdot\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{C,H_2O}}}\cdot D_{\mathrm{C,H_2O}}$$

for a cavity in the copper, mS_Z, mS_{Cu} and mS_{C} being the mass stopping powers for medium Z, copper and carbon respectively.

Taking mass energy absorption coefficients for ^{60}Co from Evans (1968) and mass stopping power values for electrons of ~10 keV from Berger and Seltzer (1964), the various equilibrium dose ratios are then as follows:

1. Air-filled cavity in copper relative to air-filled cavity in carbon (analagous to the original measurement conditions, Dutreix *et al.*, 1962):

$$\frac{{}_{\mathrm{Cu}}D_{\mathrm{air}}}{{}_{\mathrm{C}}D_{\mathrm{air}}}=\frac{mS_{\mathrm{C}}}{mS_{\mathrm{Cu}}}\cdot\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{C}}}=1.39.$$

2. Water-filled cavity in the copper relative to the equilibrium dose in water (Dutreix and Bernard, 1966):

$$\frac{{}_{\mathrm{Cu}}D_{\mathrm{H_2O}}}{D_{\mathrm{H_2O}}}=\frac{mS_{\mathrm{H_2O}}}{mS_{\mathrm{Cu}}}\cdot\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{H_2O}}}=1.45.$$

3. Air or muscle-filled cavities within the copper relative to the equilibrium dose in carbon (Spiers, 1969):

$$\frac{{}_{\mathrm{Cu}}D_{\mathrm{air}}}{D_{\mathrm{C}}}=\frac{mS_{\mathrm{air}}}{mS_{\mathrm{Cu}}}\cdot\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{C}}}=1.36.$$

$$\frac{{}_{\mathrm{Cu}}D_{\mathrm{muscle}}}{D_{\mathrm{C}}}=\frac{mS_{\mathrm{muscle}}}{mS_{\mathrm{Cu}}}\cdot\frac{\mu_{\mathrm{Cu}}}{\mu_{\mathrm{C}}}=1.59.$$

The ratios derived in 1 and 2 above are, as far as can be ascertained, identical to those presented by Dutreix *et al.* (1962), and Dutreix and Bernard (1966), while the value shown by Spiers (1969) corresponds to the mean of the air and muscle values.

The original figures are thus substantiated and the only "error" would appear to lie in Lowe's somewhat idiosyncratic interpretation.

Yours, etc.,
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REFERENCES

BERGER, M. J., and SELTZER, S. M., 1964. Tables of energy losses and ranges of electrons and positrons. *NASA report NASA SP 3012.*

DUTREIX, J., DUTREIX, A., and BERNARD, M., 1962. Etude de la dose au voisinage de l'interface entre deux mileux de composition atomique différente exposés aux rayonnement du ^{60}Co. *Physics in Medicine and Biology*, 7, 69–82.

DUTREIX, J., and BERNARD, M., 1966. Dosimetry at interfaces for high energy X and gamma rays. *British Journal of Radiology*, *39*, 205–210.

EVANS, R. D., 1968. X-ray and γ-ray interactions. In *Radiation Dosimetry* Ed. F. H. Attix and W. C. Roesch, Vol. I, pp. 93–155 (Academic Press, New York).

LOWE, D., 1978. Interface dosimetry. Letter to the Editor, *British Journal of Radiology*, *51*, 60.

SPIERS, F. W., 1969. Transition zone dosimetry. In *Radiation Dosimetry*, Ed. F. H. Attix, W. C. Roesch and E. Tochilin, Vol. III, pp. 809–867 (Academic Press, New York).

Metrizamide in hysterosalpingography

THE EDITOR—SIR,

We have recently had the opportunity of using metrizamide (Amipaque) during routine hysterosalpingography. It was used alternatively with Dimer-X in 44 patients.

The metrizamide was dissolved using 4.7 ml of solvent with 3.75 g of metrizamide, giving an iodine concentration of 280 mg per ml—the same as Dimer-X.

Assessment of the ease of injection, radiographic density and the quality of pictures in the two groups showed no significant difference. Patients were asked 30 min after the examination, whether they had any discomfort in the abdomen, and this was graded by the patient as in Table I.

Metrizamide requires a short time to prepare before the examination, which is particularly disadvantageous if more contrast is needed during an examination, above that originally prepared. The other disadvantage of metrizamide is its expense, but it may be that in the future cost per dose will be reduced.

Apart from these disadvantages, we feel that both these contrast media are suitable for hysterosalpingography, and

TABLE I

ABDOMINAL DISCOMFORT, AS GRADED BY PATIENT, 30 MIN AFTER THE EXAMINATION

	Dimer-X	Metrizamide
Severe	0	0
Moderate	2	2
Slight	6	7
Nil	14	13

that there is no difference between them with regard to quality of radiographs, ease of injection or peritoneal irritation.

We are grateful to Nyegaard & Co. A.S., for providing us with the metrizamide for this study.

Yours, etc.,
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(*Received December, 1978*)

Book reviews

Radiological Atlas of Biliary and Pancreatic Disease. By H. Baddeley, D. J. Nolan, and P. R. Salmon, pp. 218 illus., 1978 (HM & M Publishers Ltd., Aylesbury) £18·00. ISBN 0-85602-054-0.

The last few decades have witnessed great advances in gastroenterology. Improved imaging techniques have played a large part in this and their impact has been especially great on diseases of the liver and pancreas. Many of the techniques, such as endoscopic retrograde cholangiopancreatography, ultrasonography and computerized tomography, are new and not yet covered in textbooks. This atlas aims to fill the need for a book on the appearances of the biliary system and pancreas obtained both by the established and the newer techniques. The structure of the atlas is well conceived: it is divided into two sections, on the biliary system and on the pancreas. Each section has brief descriptions of the clinical presentation of the diseases followed by accounts of the radiological techniques available for their investigation. Chapters on normal appearances and congenital abnormalities are followed by systematic accounts of the major groups of diseases.

What then are the requirements of a radiological atlas and how well does this book fulfill them ? First, descriptions of the available imaging techniques and of both the normal anatomy and common congenital variants are obviously needed. These are well covered. However, the inclusion of descriptions of scintiscanning, ultrasonography and computerized tomography appears strange when these techniques are not illustrated in the atlas (apart from four pancreatic CT scans). Second, each chapter starts with brief descriptions of the diseases illustrated. These are terse and to the point although the short references to treatment are probably unnecessary in a radiological atlas. However, the authors have defined the indications for each technique and the appropriate order of investigation. The authors' bias sometimes shows through here! Many would disagree that ERCP is the investigation of first choice in a patient with bile duct cancer (p. 126). Third, an atlas must be comprehensive. The authors have certainly achieved this, collecting together both common diseases and a fascinating array of rarities. Finally, the quality of reproduction of the pictures should be good—it is.

This book ably measures up to the requirements and only minor criticisms can be made. It fills the gap as a well-written atlas of the biliary system and pancreas and should be a popular reference book for both the gastroenterologist and the radiologist.

J. A. SUMMERFIELD.

Pathology in Computed Tomography of the Brain. By Scott D. Henderson, pp. xi + 197, illus.. 1978 (Charles C. Thomas, Springfield, Illinois), $17.50.

This atlas of pathological lesions of the brain demonstrable by CT is intended to be a reference guide for all persons concerned with cranial computer assisted tomography. The author is the senior computer tomography technician at the Rush-Presbyterian-St. Luke's Medical Center in Chicago. The book consists of 19 short chapters containing 800 illustrations of the CT appearances of the commoner lesions of the brain and orbits. Each chapter has a paragraph or two of introduction and the illustrations, six to a page, are accompanied by brief legends on most of the pages. The quality of the illustrations are, on the whole, fairly good but those intended to show a variety of orbital lesions are of rather poor quality. Disconcertingly, the first chapter on cerebral atrophy contains a series of illustrations with no legends and it is difficult for those unfamiliar with CT images of the brain to tell whether they show a series of scans of the same patient or selected levels from different patients. There are no illustrations of a normal CT examination for comparison with the abnormal scans. This would help the atlas to fulfil its intended purpose, an introduction for beginners to this relatively new diagnostic method.

Many of the legends for the figures are cryptic and a lot of space which could have been devoted to describing the images is wasted in over-elaborate acknowledgments to the sources of some of the material. The pages are numbered only at the beginning of each chapter which makes quick reference to a particular section rather difficult.

The publishers state that this atlas will "greatly facilitate learning and will continue to serve the tomography technician, resident and practising radiologist as a reference of unparalleled comprehensiveness and clarity".

Even when allowance is made for publishers hyperbole this has not been achieved nor, I am sure, was it the aim of the author to do so. Mr. Henderson is to be congratulated on his initiative in writing this atlas and for a good first try. Should a second edition be contemplated fewer illustrations of better quality, inclusion of a normal CT examination, a more lengthy introduction to each chapter and more lucid legends for the illustrations would greatly enhance its value as an introduction for both radiographers and trainee radiologists to cranial computer assisted tomography.

T. D. HAWKINS.

1979, *British Journal of Radiology*, *52*, 423–424 May 1979

Proceedings of The British Institute of Radiology

Principles of clinical trials in cancer

Abstracts of papers presented at a meeting of The British Institute of Radiology held on Thursday, October 19, 1978 at the Institute House, 32 Welbeck Street, London W1M 7PG.

Surgical and clinical aspects of some clinical trials, by M. Baum.
Comments on the feasibility, practicability and success rate of breast screening, by Audrey Tucker.
Comments on the statistical approach and the interpretation of results, by K. D. MacRae.

SURGICAL AND CLINICAL ASPECTS OF SOME CLINICAL TRIALS

By M. Baum

Welsh National School of Medicine

Prospective randomized clinical trials are in their relative infancy but are an essential technique in the application of the scientific method to the treatment of cancer. By this technique not only is it possible to compare competing hypotheses concerning the disease, but by their scientific design there is inevitably a biological fall-out which teaches us more about the very nature of the disease under study, and hence enables us to evolve even more rational treatment programmes. Clinical trials for cancer can be conducted in a single centre or as a multi-centre collaborative programme. Single centre trials have the advantage of tight control, excellent data collection, and the possibility of complicated protocols.

However, multicentre trials have the overwhelming advantage in that they allow the rapid accrual of large numbers of patients, but by their very nature control may be less tight and only simple protocols are appropriate. The most important point to consider when planning a multicentre trial is the number of patients that are required to answer the question posed. For example, in setting up a trial that stands a 90% chance of picking up a significant difference of the order of say 10% (the power of the trial), at least 500 patients will be required in each treatment arm. The recruitment and co-ordination of such enormous studies demands special expertise, and the expense of full-time co-ordinators and administrators. Protocols have to be carefully designed so that the question is clearly defined, the treatment modality carefully described, and the possibility of treatment interaction avoided. Examples were given concerning a variety of multicentre prospective trials investigating the treatment of breast cancer, some of which have influenced current thought and management concerning this disease. Thus local therapy by whatever type of operation and covering a wide range of radiotherapy regimes has not influenced survival but may provide different degrees of local control.

New adjuvant trials to investigate chemotherapy or endocrine therapy at the time of mastectomy are under evaluation at the present, but the new problem arises in defining what is an optimum chemotherapy regime when dealing with micrometastases whose very presence and growth rate can only be guessed. Details concerning documentation, randomization procedures and communication techniques were described, followed by discussion on the ethics of informed consent, and the timing of closing a trial. It is felt that in all honesty there is no such thing as true informed consent and that the attitude of the Medical Research Council on this issue is the most humane.

American attitudes on this subject are not particularly relevant to British practice. Finally, the expense of running a properly organized prospective trial was described. It has to be considered a very costly business which needs to be funded adequately. However, to keep the subject in perspective, the cost of saving a life of a woman as a result of a wide scale screening programme would pay for at least one large scale multicentre trial, that would be likely to detect an improvement with a new treatment regime of the order of 10%. This improvement extrapolated across the country could then save around 800 lives a year.

COMMENTS ON THE FEASIBILITY, PRACTICABILITY AND SUCCESS RATE OF BREAST SCREENING

By Audrey Tucker

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It is generally known that the commonest cause of death in women aged 40–65 from malignancy in England is carcinoma of the breast.

Methods of breast screening include self palpation, palpation by clinicians, thermography and X-ray mammography. Of these methods, mammography detects a much higher percentage of occult (not clinically overt) carcinomata. Such women have a much lower incidence of axillary node involvement, and detection prior to spread to axillary nodes is the only factor at present known to give a significantly better prognosis. Most of the cancers found are also smaller than those presenting as lumps.

In the series from Lundgren (Sweden), 112 out of 129 carcinomata found by X-rays had normal axillary nodes. In a series at present being undertaken in England, 23 out of 30 women had no axillary lymph node involvement.

Breast sensitivity to ionizing radiation is known to be much greater below the age of 35, and therefore screening should not start before this age. Any breast X-rays must be taken with the lowest irradiation dose compatible with good diagnostic films; compression helps to reduce the dose.

There is no evidence at present, other than extrapolated estimates from very high (radiotherapy) dosages that mammography within the diagnostic range could cause breast cancer; but interval rather than annual mammography is probably advisable for normal women and those not in high risk groups.

Mammography is easily performed, and not very expensive. However, with nearly nine million women in Britain between the ages of 40–65, many more radiologists than are available would be needed to interpret the films of a national screening programme.

COMMENTS ON THE STATISTICAL APPROACH AND THE INTERPRETATION OF RESULTS

By K. D. MacRae

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Only by the use of randomization can a clinical trial be validly said to be a controlled trial; randomization eliminates allocation bias, ensures that the treatment groups

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tend to be balanced for predictor factors, and makes the use of statistical tests of significance valid (Byar *et al.*, 1976).

A useful clinical trial must also have an adequate number of patients to ensure that differences between alternative treatments that would be of interest to those in clinical practice are likely to be detected by the trial. Small clinical trials are of very limited value, whether or not they show significant differences between the treatments, because they allow only vague statements about the likely magnitude of the treatment differences to be made. When to stop a clinical trial often poses an ethical and scientific dilemma, and perhaps the only way of dealing with this problem is for the clinicians treating the patients to remain ignorant of the intermediate results and for a close scrutiny to be kept on the data by a suitably constituted group of assessors (Chalmers *et al.*, 1972).

It is also necessary that the question being asked in a clinical trial should not be wrongly put; examples of confounded comparisons have occurred in some major trials in the past, and factorial trials are almost unknown in the field of breast cancer.

REFERENCES

BYAR, D. P., SIMON, R. M., FRIEDEWALD, W. T., SCHLESSELMAN, J. J., DEMETS, D. L., ELLENBERG, J. H., GAIL, M. H., and WARE, J. W., 1976. Randomized clinical trials. *New England Journal of Medicine, 295*, 74–80.

CHALMERS, T. C., BLOCK, J. B., and LEE, S., 1972. Controlled studies in clinical cancer research. *New England Journal of Medicine*, *287*, 75–78.

The scientific basis of radiation protection

Abstracts of papers presented at a Radiobiology Work-in-Progress meeting of The British Institute of Radiology held on October 20, 1978 in the Reid-Knox Hall, Institute House, 32 Welbeck Street, London W1M 7PG.

An introduction to "The Scientific basis of radiation protection", by R. H. Mole.
Chromosome damage: the RBE of (d + T) neutrons from two different generators, by Gillian Clare, C. Oxby and B. Dixon.
Low doses of neutron radiation and the frequency of satellite association complexes of human acrocentric chromosomes, by M. T. Khokhar, T. Min and J. A. Houghton.
Accurate quantification of radiation-induced chromosome damage in human lymphocytes utilizing the harlequin-banding technique: implications for biological dosimetry, by D. Scott, C. Y. Lyons, J. R. Robinson and A. R. Currie.
Fast kinetics of radioprotection by sulphydryl compounds in bacteria, by H. A. Harrop and B. D. Michael.
Mechanisms of radioprotection by L-cysteine or cytosine arabinoside in mouse marrow, by J. L. Millar.
A method for measuring the effects of plutonium 239 on cells in haemopoietic marrow, by E. R. Humphreys and V. A. Stones.
An alternative bone model in the calculation of annual limits of intake for plutonium 239 compounds, by N. D. Priest.
The initial deposition and redistribution of plutonium 239 in the mouse skeleton: implications for rodent studies in plutonium 239 toxicology, by D. Green, G. R. Howells and C. M. Thorne.
Skin and eye irradiations—examples of some problems of implementing international recommendations in radiological protection, by M. W. Charles.
The scientific basis for the ICRP's use of linear extrapolation to obtain best estimates of the risk of radiation-induced cancer at low doses, by J. M. Brown.

AN INTRODUCTION TO "THE SCIENTIFIC BASIS OF RADIATION PROTECTION"

By R. H. Mole

Medical Research Council Radiobiology Unit, Harwell, Oxon

Chemical agents reducing effects of radiation could well be called radio-resistizers (by analogy and in contrast with radio-sensitizers). Radiation protection is a misnomer for their action.

Radiobiological protection is an activity maintaining conditions which minimize exposure to ionizing radiation. Its scientific basis is the field of knowledge, both facts and concepts, which allows risk to be defined quantitatively for any and every kind of exposure. Since human experience of radiation risk is limited to particular cases, the available information has to be codified before it can be applied to other circumstances, absorbed dose providing the necessary linking concept. The effect of protraction (rather than physical dose-rate which is relevant to low LET radiation but not high LET radiation) and of radiation quality are the two main quantitative problems if the metabolic models in use for assessment of dose from "internal emitters" can be accepted as adequate, but the non-stochastic concept of a graded reduction in organ function requires much more precise definition than ICRP has given it. Radiobiological experiments are of applied value only if they lead to defensible generalizations which are applicable to the human species. A system of radiological protection, because it must be simple enough for practical use, must also involve considerable simplification of inevitable biological complexity but simplification is a matter for judgement, not primarily of science. The increased emphasis on cost-benefit analysis in ICRP Publ. 26 (1977) demands a considerably increased effort if all the realistic risk estimates which are needed are to be provided.

REFERENCE

ICRP, 1977. Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP, Publication 26.*

CHROMOSOME DAMAGE: THE RBE OF (d+T) NEUTRONS FROM TWO DIFFERENT GENERATORS

By Gillian Clare, C. Oxby and B. Dixon

University Department of Radiotherapy, Cookridge Hospital and University Department of Medical Physics The General Infirmary, Leeds

Human blood has been irradiated *in vitro* at 22°C with ^{60}Co γ rays at 1.5 Gy min^{-1} or 0.006 Gy min^{-1}, or with 14 MeV

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neutrons given either continuously (Philips tube, 0.11 Gy min^{-1}) or in 15 μsec pulses at a rate of two per second (Elliott tube, cumulative dose-rate of 0.006 Gy min^{-1}). Metaphases from lymphocytes stimulated with PHA were scored either at the first division for gross chromosomal aberrations and "extra fragments", or for sister chromatid exchanges (SCE) after two divisions in medium containing 5-bromode-oxyuridine.

After γ-irradiation (0-8 Gy) the response for dicentrics and rings was composed of a linear and a dose-squared component. For "extra fragments" up to 3.0 Gy, and SCE's (0-7 Gy), the response curves were linear. Cells were also irradiated with 3 MeV electrons at 306 Gy min^{-1}, or 3 MeV X rays at 236 Gy min^{-1} during each 2 μsec pulse. The numbers of dicentrics and rings were not significantly greater than those induced by γ rays.

After neutron irradiation, for gross chromosomal aberrations, "extra fragments" and SCE's, all dose-response curves were linear. The RBE relative to ^{60}Co γ rays for gross chromosomal aberrations varied from 5.4 to 2.6 (0–0.8 Gy from the Elliott tube), which was about twice as high as the RBE obtained with the Philips tube (0–2.4 Gy), which varied from 2.9 to 1.4. The RBE, using neutrons from the Philips tube, for SCE's was 2.3 ± 0.5. The RBE, using neutrons from both tubes, for "extra fragments" was 2.1 ± 0.4.

In conclusion, gross chromosomal aberrations appear to be a more accurate indicator of dose than "extra fragments" and both are four times more sensitive indicators of dose than SCE's.

LOW DOSES OF NEUTRON RADIATION AND THE FREQUENCY OF SATELLITE ASSOCIATION COMPLEXES OF HUMAN ACROCENTRIC CHROMOSOMES

By M. T. Khokhar, T. Min and J. A. Houghton

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University College, Galway, Ireland

The human acrocentric chromosomes may often be observed associated together or aligning themselves with their satellites directed towards each other and in close proximity. It has been suggested that this phenomenon of satellite association (s.a.) may be one of the determining factors in the causation of non-disjunction in man. Down's syndrome, the most common human autosomal disorder, is usually caused by non-disjunction of chromosome 21. The incidence of Down's syndrome has been found to be higher among the children of parents who have been exposed to ionizing radiation for radiotherapeutic or radiodiagnostic reasons. To determine whether irradiation leads to an increased incidence of s.a. and, therefore, an increased risk of chromosome non-disjunction, the frequency and patterns of satellite associations in metaphase preparations of irradiated blood samples were investigated. Cobalt 60 gamma rays did not indicate a dose response effect on the frequency of s.a. of the acrocentric chromosomes (Khokhar *et al.*, 1978).

The effects of neutrons have also been studied. Blood samples were irradiated with Hammersmith neutrons giving doses of 0.04, 0.08, 0.16, 0.24, 0.48 and 0.96 Gy and the metaphase preparations were G-banded. The metaphases were analysed to determine if there was any selective effect of neutron irradiation on the individual acrocentric chromosomes participating in the formation of s.a. complexes. Analysis of the preliminary data indicates that chromosome 13 associates with higher frequency than chromosomes 14, 15, 21 or 22.

REFERENCE

Khokhar, M. T., Min, T. and Houghton, J. A., 1978. A study of the effects of very low doses of cobalt 60 gamma rays on the frequency of satellite association of human acrocentric chromosomes. *British Journal of Radiology*, *51*, 559–560.

ACCURATE QUANTIFICATION OF RADIATION-INDUCED CHROMOSOME DAMAGE IN HUMAN LYMPHOCYTES UTILIZING THE HARLEQUIN-BANDING TECHNIQUE: IMPLICATIONS FOR BIOLOGICAL DOSIMETRY

By D. Scott, C. Y. Lyons, J. R. Robinson and A. R. Currie

Paterson Laboratories,
Christie Hospital and Holt Radium Institute,
Manchester M20 9BX

The frequency of chromosome structural aberrations in peripheral blood lymphocytes of radiation-exposed individuals is used in biological dosimetry by referring to dose-response curves constructed from *in vitro* exposure of blood samples. From the shapes of these dose-response curves, predictions are also made of the effect of dose-rate on aberration frequency and the mechanisms of aberration formation.

Lymphocytes must be examined at their first post-irradiation mitosis in order to quantitate accurately the chromosome damage. Using the new harlequin-banding technique of bromodeoxyuridine (BUdR) treated cells we have shown, as have others, that the assumption of a pure first-division population after 48h of culture is erroneous; as many as 50% of cells may be in second division at this time. A further assumption which is made in using a 48h sample is that first-division cells at this time carry the same amount of damage as cells undergoing first division at other times, *i.e.* that the G_0-irradiated lymphocyte population is homogeneous in chromosomal radiosensitivity. This latter assumption has been shown to be correct by culturing irradiated cells in a BUdR-containing medium and sampling cells at various post-irradiation intervals. Correct dose response curves can therefore now be obtained over a wide range of sampling times by utilizing this technique and confining observations to non-harlequin-banded (*i.e.* first division) cells.

FAST KINETICS OF RADIOPROTECTION BY SULPHYDRYL COMPOUNDS IN BACTERIA

By H. A. Harrop and B. D. Michael

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We have used a fast mixing and irradiation technique, the gas explosion method, to resolve some of the processes by which *serratia marcescens* chemically repairs radiation-induced oxygen-dependent damage. The kinetics of the decay of damage (*i.e.* its chemical repair) display fast and slow stages. These are well fitted by a model in which there are two components of damage, each repaired as an exponential function of time, but differing in repair rate by a factor of ten. In the present work the interaction of these components with the sulphydryl radioprotector dithiothreitol (DTT) has been examined. The addition of DTT was found to increase the rates of decay of both the fast and the slow components of damage. Four concentrations of DTT were tested in the range 0.5 to 5.0 mM and it appeared that the increase of fast and slow decay rates were proportionately the same at each concentration. A linear relationship was found between DTT concentration and repair rate. The reaction rates of DTT repair were determined to be 3.6 and 0.36×10^6 dm $\text{mol}^{-1}\text{s}^{-1}$ for the fast and slow components respectively ◆

assuming that the intracellular and extracellular concentration of DTT are equal. These rates are comparable with, although somewhat slower than, those that have been determined for free radical repair by DTT using the pulse radiolysis technique (Redpath, 1973).

When the bacteria were pretreated and irradiated with the sulphydryl binding agent, N-ethylmaleimide (NEM), the lifetimes of both components were decreased by at least a factor of two. The effect of the NEM on the lifetimes of the oxygen-dependent damage could be reversed by adding glutathione to the previously NEM-treated bacteria.

It was thus possible to increase or decrease the rate of repair of *serratia marcescens* by augmenting or depleting the pool of reducing substances in the cell.

REFERENCE

Redpath, J. L., 1973. Pulse radiolysis of dithiothreitol. *Radiation Research*, *54*, 364–374.

MECHANISMS OF RADIOPROTECTION BY L-CYSTEINE OR CYTOSINE ARABINOSIDE IN MOUSE MARROW

By J. L. Millar

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Mice given 1000 rad total body irradiation die 10 to 14 days later as a result of reduced output of essential blood elements from the bone marrow. If, however, the animals are given 200 mg/kg cytosine arabinoside (ARA-C) two days before radiation the animals survive. The improved survival results from a more rapid recovery of peripheral blood elements in pretreated mice. This suggests that the vital bone marrow stem cells which produce these cells are protected by ARA-C pretreatment. This is not the case, however, as ARA-C pretreatment does not alter the radiosensitivity of the stem cells. It is the subsequent recovery of the stem cells in ARA-C pretreated animals that is altered. In animals receiving radiation alone, there is a post irradiation lag phase of several days during which there appears to be no increase in haemopoietic stem cell number. ARA-C abolishes this lag phase and recovery of the stem cells begins immediately after the irradiation.

This is in contrast to the mechanism by which cysteine protects animals. This compound produces a genuine dose reduction effect, so more cells survive irradiation. These surviving stem cells show no evidence of enhanced recovery and follow the pattern of regeneration in the irradiated controls. We conclude, therefore, that there is a qualitative difference in the ways in which ARA-C and cysteine protect animals from a large dose of radiation that would normally prove lethal.

A METHOD FOR MEASURING THE EFFECTS OF PLUTONIUM 239 ON CELLS IN HAEMOPOIETIC MARROW

By E. R. Humphreys and V. A. Stones

MRC Radiobiology Unit, Harwell, Oxon OX11 0RD

A technique is described which is being used to investigate whether the plutonium which deposits on the endosteum in bone irradiates those marrow cells involved in the early stage of haemopoiesis.

Mice were given about 300 Bq ^{239}Pu intravenously and injected three days later with 550 kBq [^{125}I]-5-iodo-2′-deoxyuridine. The ^{125}I-labelled marrow cells harvested from the femur shafts of these donors after 24h are then injected into lethally irradiated (10 Gy X rays) syngeneic hosts. The activity in the ^{125}I-labelled colonies established in the spleens of the hosts is then measured at intervals over several days and the results analysed to give a measure of haemopoietic stem cell numbers in the injected marrow cells (Siegers *et al.*, 1979).

Preliminary results comparing ^{125}I activity in spleens measured six and eight days after transplantation of cells from control and ^{239}Pu-treated donors showed that an absorbed dose of about 0.1 Gy depressed marrow cell numbers two or threefold.

REFERENCE

Siegers, M. P., Feinendegen, L. E., Lahiri, S. K. and Cronkite, E. P., 1979. Relative number and proliferation kinetics of haemopoietic stem cells in the mouse. *Blood Cells* (in press).

AN ALTERNATIVE BONE MODEL IN THE CALCULATION OF ANNUAL LIMITS OF INTAKE FOR PLUTONIUM 239 COMPOUNDS

By N. D. Priest

National Radiological Protection Board, Harwell, Oxon

Annual limits for the intake (ALI) of ^{239}Pu are calculated by Committee 2 of ICRP using a dosimetric model which incorporates a skeletal model for bone surface seeking radionuclides (ICRP, 1979). The skeletal model assumes plutonium is evenly deposited as an infinitely thin layer over bone surfaces and retained with a half-time of 100 years. This model is conservative because it takes no account of the burial of plutonium during bone remodelling. This burial greatly reduces the amount of α-energy absorbed by the sensitive cells in the skeleton. Consequently, the ALI's calculated using the ICRP bone model are unnecessarily restrictive.

For the present paper ALI's have been calculated using a multicompartment skeletal model which allows for plutonium burial and recycling (Priest and Hunt, 1978). In one compartment of this model, the growing surfaces of cortical bone, it is assumed that plutonium deposits are retained and are not subject to recycling. In other compartments plutonium is taken to be resorbed with subsequent redeposition on to bone surfaces or retention in the bone marrow. The calculations made using this model suggest that 750 Bq (20 nCi) is an appropriate ALI for the inhalation of plutonium compounds and that 830 kBq and 5 MBq (23 μCi and 136 μCi) are the appropriate ALI's for the ingestion of soluble and insoluble forms of plutonium respectively. These ALI's are 1.5–3.0 times less restrictive than the ALI's which will be published by Committee 2 of ICRP.

REFERENCES

ICRP, 1979. Limits for intakes of radionuclides by workers. Report of the ICRP Committee 2. (In press).

Priest, N. D. and Hunt, B. W., 1978. The calculation of annual limits of intake for plutonium-239 in man using a bone model which allows for plutonium burial and recycling (unpublished).

THE INITIAL DEPOSITION AND REDISTRIBUTION OF PLUTONIUM 239 IN THE MOUSE SKELETON: IMPLICATIONS FOR RODENT STUDIES IN PLUTONIUM 239 TOXICOLOGY

By D. Green, G. R. Howells and M. C. Thorne

MRC Radiobiology Unit, Harwell, Oxfordshire, OX11 0RD

Using neutron-induced autoradiography together with computer-based methods of data reduction (Green *et al.*, 1977) the distribution of ^{239}Pu about the endosteal and periosteal surfaces of bone can be measured with a resolution of $\pm$ 2.5 μm. Our studies show that in the female CBA mouse the ^{239}Pu penetrates up to 20 μm into the bone 24 hours after intravenous injection of monomeric ^{239}Pu-citrate.

Studies on the ilium demonstrate that after this period of initial deposition the ^{239}Pu is gradually redistributed throughout the bone and its included marrow. It is suggested that the burial of ^{239}Pu in bone is governed entirely by the process of bone accretion and that its long term retention in marrow is in fixed tissue macrophages.

Blood flow experiments using ^{18}F have also been performed. These suggest the hypothesis that the initial deposition of ^{239}Pu in the various bones of the skeleton can be accurately predicted from a knowledge of the surface-to-volume ratios of these bones and the blood flow to them.

It is pointed out that if ^{239}Pu deposition in the skeleton is governed by blood flow to and morphological characteristics of the bones and if its redistribution is governed entirely by mechanisms of bone turnover, it should be possible to construct a satisfactory physiological model of ^{239}Pu deposition and redistribution in the human skeleton from clinical data which are already potentially available.

REFERENCE

Green, D., Howells, G. R. and Thorne, M. C., 1977. A new method for the accurate localization of ^{239}Pu in bone. *Physics in Medicine and Biology*, *22*, 284–297.

SKIN AND EYE IRRADIATIONS—EXAMPLES OF SOME PROBLEMS OF IMPLEMENTING INTERNATIONAL RECOMMENDATIONS IN RADIOLOGICAL PROTECTION

By M. W. Charles

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Publication 26 of the International Commission on Radiological Protection (ICRP, 1977) provides a rationalized radiation protection system, through the use of up-to-date stochastic risk factors, which avoids some of the inconsistencies of earlier recommendations. It has introduced the concepts of stochastic and non-stochastic phenomena and the evaluation of detriment rather than just lethality as a measure of harm. These concepts will no doubt continue to evolve as the ICRP's recommendations have done in the past.

Some areas where further discussion and experimental radiobiology would be pertinent are sometimes apparent to the health physicist who applies international recommendations in operational situations. In practice, for example, the skin may sometimes be subjected to non-uniform irradiation with radioactive sources of dimensions from several centimetres down to a few microns. Peak dose rates in the basal layer may be several tens of Gy h^{-1} but, due to the spatial non-uniformity of the exposures, the mean dose rate over some arbitrary area such as 1 cm^2 may be several orders of magnitude less. The outcome of such exposures is not well-known and ICRP 26 (para. 183) gives little guidance on their treatment. Whole-body skin exposures are limited, by non-stochastic effects, to life-time dose equivalents of 20 Sv (2000 rem); skin is considered to be much less liable to develop fatal cancer than other tissues (ICRP 26, para. 63). However, since the incidence of skin cancer may not be negligible (Shore *et al.*, 1976), and since its magnitude is presumably required for the evaluation of detriment, stochastic effects in skin should not be altogether forgotten.

Evaluation of detriment is, however, complex and a case can be made for considering basal cell carcinoma as a pseudo non-stochastic effect, much as Malone (1978) has suggested for benign neoplasia in the thyroid. In the case of the eye the annual maximum permissible dose has been increased from 0.15 to 0.3 Sv (15-30 rem). A lifetime dose-equivalent of 15 Sv (1500 rem) is considered to be below the threshold for cataract induction (ICRP 26, para. 61). This value appears to leave little, if any, margin of safety compared with the threshold doses indicated in some clinical studies with low and high LET radiation (Merriam *et al.*, 1972; Roth *et al.*, 1976). The extent of sparing for protracted cataractogenic exposures remains an important parameter for continued study.

REFERENCES

ICRP, 1977. Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP, Publication 26.*

Malone, J. F., 1978. Thyroid irradiation and the new ICRP dose limits. *British Journal of Radiology*, *51*, 553–556.

Merriam, G. R., Szechter, A., and Focht E. F., 1972. The effects of ionizing radiations on the eye. *Frontiers of Radiation Therapy and Oncology*, *6*, 346–385.

Roth, J., Brown, N., Catterall, M. and Beal, A., 1976. Effects of fast neutrons on the eye. *British Journal of Ophthalmology*, *60*, 236–244.

Shore, R. E., Albert, R. E. and Pasternack, B.S., 1976. Follow up study of patients treated by X-ray epilation for tinea capitis. *Archives of Environmental Health*, *31*, 21–28.

THE SCIENTIFIC BASIS FOR THE ICRP'S USE OF LINEAR EXTRAPOLATION TO OBTAIN BEST ESTIMATES OF THE RISK OF RADIATION-INDUCED CANCER AT LOW DOSES

By J. M. Brown

Stanford University and
MRC Unit of Clinical Oncology and Radiotherapeutics
Hills Road, Cambridge

In its latest recommendations on radiation protection, the International Commission on Radiological Protection has published estimates of the risk of developing cancer folowing low doses and dose rates of radiation (ICRP, 26, 1977). These are to be considered "best estimates" of the risk at low doses, and as such represent a break from the traditional view that risk estimates derived from linear extrapolation are likely to overestimate the real risk at low doses.

The basis for this judgement is that the shape of the dose response curve at low to moderate doses is likely to be of the form:

$$E = aD + bD^2$$

where E is the effect at dose D and "a" and "b" are constants. To derive values of a/b (dose at which the linear and quadratic terms contribute equally to the response), it is assumed that the initiating event for radiation carcinogenesis is a somatic mutation. A summary of the values of a/b obtained for mutations and 2-hit chromosome aberrations in the literature shows that they cluster around 100 rad for mammalian cells. Thus, if this applied to cancer induction the dose-response curve would be predominantly linear from 0 to 100 rad. An analysis of risk estimates for radiation-induced cancer in man supports this prediction.

REFERENCE

ICRP, 1977. Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP, Publication 26.*

Forthcoming events and other notices

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Conversazione

The British Institute of Radiology Conversazione will be held at the new Royal College of Radiologists house at 38 Portland Place, London on May 16, 1979.

Further information from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

Containing Laboratory Hazards

A conference to be held on May 16, 1979 at the Kensington Palace Hotel, London W8. The distinguished panel of speakers includes Clive Jenkins, General Secretary of the ASTMS, and other experts in the field of safety and health. They will highlight the practical problems and solutions to laboratory safety. Details from European Study Conferences Ltd., 31 High Street, East Uppingham, Rutland LE15 9PY.

Mackenzie Davidson Memorial Lecture

To be given by Dr. G. B. Schofield, Medical Officer, British Nuclear Fuels Ltd., on *Biological control in a plutonium production facility* at The British Institute of Radiology, 32 Welbeck Street, London W1 on Thursday, May 17, 1979.

Paediatric Radiology

A two-day course in diagnostic paediatric imaging will be held at the Institute of Child Health, Hospital for Sick Children, Great Ormond Street, London WC1 on May 17–18, 1979. The main theme of this course will be the thorax.

Further details and application forms are available from The Secretary, Department of Paediatric Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JN.

Postgraduate Weekend Course in Radiotherapy and Oncology

A meeting organized by the Royal College of Radiologists to be held on Saturday, May 19, 1979 at the Edward Lewis Theatre, Medical School, Middlesex Hospital, London.

Further information from the Royal College of Radiologists, 38 Portland Place, London W1N 3DG.

International Symposium on Interventional Radiology

An EAR Symposium, organized by the Portuguese Society of Radiology and Nuclear Medicine, will be held May 30–June 2, 1979 in the Algarve, Portugal.

Proposed sessions include vascular therapy; selective embolization and management; catheter implantation in chemotherapy and percutaneous treatments; ultrasonic guiding techniques and nuclear imaging as a guiding technique for biopsy and fluid aspiration.

For further information contact the Portuguese Society of Radiology and Nuclear Medicine, 123, 1.° Esq., Avenida Elias Garcia, Lisbon 1, Portugal.

Nuclear Cardiology

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology to be held on June 20, 1979 at St. Bartholomew's Hospital, Gloucester House, Little Britain, London EC1. Anyone wishing to make a presentation should contact Dr. K. E. Britton, St. Bartholomew's Hospital.

Further information regarding this meeting can be obtained from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

European Symposium on Radiopharmacology

To be held at Noordwijkerhout (The Netherlands) June 21–23, 1979.

This symposium will be held under the auspices of The European Nuclear Medical Society, The Society of Nuclear Medicine (Die Gesellschaft für Nuklearmedizine) and The Department of Nuclear Medicine Rotterdamsch Radio-Therapeutisch Instituut, Groene Hilledijk 301, 3075 EA Rotterdam, Head of the Department: Dr. P. H. Cox.

Sessions will be held on ionic tumour localizing radiopharmaceuticals, technetium Hida derivatives for liver function investigations and technetium skeletal scanning reagents.

Early registration is recommended as participation will be limited to 200 participants.

For further details and registration please contact: Dr. P. H. Cox, Head of Department of Nuclear Medicine, R.R.T.I. Rotterdam: Groene Hilledijk 301, 3075 EA Rotterdam, The Netherlands.

20th Summer School in Health Physics

This course being held July 2–13, 1979, provides a broad background in the subject and is particularly suited to those carrying responsibilities for radiological protection in government, industry, hospitals and education.

Details from Dr. H. D. Evans, Health Centre, Imperial College, London SW7 2AZ.

IV European Congress of Radiology

The IV European Congress of Radiology will take place in Hamburg (German Federal Republic), September 4–8, 1979.

Scientific programme:
diagnostic research of organs of the upper abdomen;
diagnostic research in nuclear medicine: organs of the upper abdomen;
radiotherapy in tumours of the genital system of males and females;
radiobiology and X-ray protection (combined therapies and risks of ray exposure);
radiophysics and techniques (methodical problems in diagnostics and in planning of radiotherapy).

Enquiries: Secretary of the IV European Congress of Radiology, Postfach 10 64 07, D-2000 Hamburg 1, Federal German Republic.

Quantitation of Tumour Response: a Critical Appraisal

The L. H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to stimulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.

Factors of prognostic significance.

In vitro assays of tumours excised after treatment *in vivo*.

The choice of suitable experimental models in rodents.

The role of human tumour xenografts.

Statistical evaluation of tumour response data.

The limitations and artefacts of each assay technique.

The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

3RD POSTGRADUATE COURSE IN RADIOLOGY

To be held in Verona, October 3–6, 1979 on kidney radiology.

The following subjects will be treated: renal malformations: specific infectious diseases; non-specific infectious diseases; renovascular hypertension; renal traumas; renal tumours; ureteropelvic junction diseases; renal calculi and obstructive syndrome; renal failure; renal transplantation; extra-renal involvement of renal pathology.

Registration fee 65000 Italian Lire (by May 31, 1979) after this date: 100000 Italian Lire.

Secretary: Radiology Department, University Hospital, Verone, Italy.

5TH INTERNATIONAL CONGRESS OF THE INTERNATIONAL RADIATION PROTECTION ASSOCIATION

Will take place in Jerusalem, Israel, March 9–14, 1980.

The scientific programme of the Congress will cover all aspects of radiation protection with emphasis on its central theme: radiation protection—a systematic approach to safety.

Free papers are invited and the deadline for abstracts is May 15, 1979.

An interesting programme has been planned including a commercial exhibition and pre- or post-congress workshops and Professional tours.

Social events and a programme for accompanying persons have been organized.

For further information: The Secretariat, 5th International Congress of IRPA., PO Box 16271, Tel Aviv, Israel.

SYMPOSIUM ON SPINE AND ITS CONTENTS

EAR "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in:

(a) Equipments and investigative methods of spine and spinal cord.
(b) Radioanatomy and physiology of spine and spinal cord.
(c) Radiodiagnosis of pathological conditions.
(d) Interventive (diapeutic) radiodiagnostic methods.

For further information contact (not later than June 1979): The secretariat of "Vertebro 1980", PO Box 88, Sokolská 31, 120 26 Praha 2, Czechoslovakia.

XV INTERNATIONAL CONGRESS OF RADIOLOGY

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Further information from: Secretariat ICR-81, Ave. Winston Churchill 234B-Box 16, B-1180 Brussels, Belgium.

Book review

The veins of the posterior fossa: normal and pathologic findings. By A. Wackenheim and J. P. Baurn. pp. xi+157, illus., 1978 (Springer Verlag, Berlin, Heidelberg, New York), DM136/$68.
ISBN 3-540-08337-5.

This work presents a review of the anatomy of the posterior fossa veins followed by an analysis of the displacement, which may be caused by masses in various situations as well as changes associated with other pathologies. The brief text is supplemented by extensive and up-to-date references to the literature.

The book is extensively illustrated with well selected subtraction angiograms supplemented with photographs and radiographs of anatomical specimens and by line drawings and other diagrams. These make the book a good teaching atlas of interest to all involved in the neurological sciences but of special value to students of neuroradiology.

B. KENDALL.

Book reviews

Origins of Human Cancer. Edited by H. H. Hiatt, J. D. Watson and J. A. Winsten, 1977 (Cold Spring Harbor Laboratory), $45.00.

Book A. Incidence of Cancer in Humans. pp. xxvi+602.

This is not a book for detailed review. It contains 42 rather varied papers of various lengths about cancer and geography, genetics, occupation, industrial, agricultural and medicinal chemicals, radiation and diet. The contributors are all well-known and their contributions often quite predictable which is not also to say that they are always quite reliable. Many papers were without conclusions and often, *pace* the title, were not about human cancer incidence at all but about the possibility of it. There was a considerable emphasis sometimes on the hypothesis that compounds found to be mutagenic in bacterial or other test systems will, or must, be carcinogenic in man, whether or not there is positive human evidence. Pollution of drinking water appeared unimportant but a large fraction of naturally occurring cancers may be attributed to aspects of "life-style", particularly foodstuffs and diet (as well, of course, as smoking). In contrast, chemical agents, whether in occupational exposure or in medicinal preparations, seemed quantitatively much less important except in individuals receiving high dosages.

The Conference Proceedings includes two more volumes of similar size on Mechanisms of Carcinogenesis and Human Risk Assessment. All this took seven consecutive days to tell before over 250 participants. The editors' preface says the programme was very, very full, the breadth of disciplines exceptional (even including policy analysis and news media), and the bringing out of the books an even more major task than envisaged. The initial and laudable premise was that cancer prevention has received much less attention than it deserves. Whether publication at length and in this form is an appropriate response can be questioned. Richard Doll's characteristically lucid and masterly introductory chapter summed up the essentials.

R. H. MOLE.

Book B. Mechanisms of Carcinogenesis. pp. to 1303.

This book is, one gathers (there is no foreword or introduction), the second of a three volume account of a meeting at Cold Spring Harbor (U.S.A.) on the Origins of Human Cancer. It is a collection of papers given at that meeting and is divided into six sections. The first (section 9 of the three volumes) deals with electrophilicity, the second deals with factors which modify carcinogenicity, the third deals with aryl hydroxylase genetics, the next section deals with damage to DNA and its repair and the last two sections deal with DNA and RNA viruses.

The book opens with an excellent chapter by the Millers on the fundamental physico-chemical properties of mutagens and carcinogens and their interrelationship. It also deals in an extremely lucid way with the Millers' concept of metabolic activation of these agents from their inactive precursors.

It would be invidious to pick out any of the chapters which follow for special mention since they are all of an enormously high standard and should be required reading for anyone who either makes decisions on carcinogenicity of compounds or engages in research on them. Nevertheless this reviewer found the chapter by Rajewsky to be of great significance since it describes in detail the organ specificity that may be expressed by one carcinogen and the conclusions which can be drawn from such high organ specificity. There is also an excellent review of the concept of immunological surveillance by Stutman which puts into critical perspective the arguments for and against this concept which held sway for a decade but is now frayed at the edges.

The book can be highly recommended not only to those engaged in research on carcinogenesis but to all those who have pretentions to understanding cancer biology.

K. HELLMAN.

Book C. Human Risk Assessment. pp. to 1888.

It is understandable that the reader of this journal, who may spend much of his time diagnosing or treating human cancer, should have more than a passing interest in the causes of this group of diseases. In 1976 the Cold Spring Harbor Laboratories held an international meeting which attempted to cover the whole area of the origin of human cancer, with the emphasis throughout on prevention. The proceedings of the meeting run to nearly two thousand pages in three volumes. The first volume focuses on the environmental factors believed to be reponsible for most cancer; the second looks in detail at the mechanisms involved. The third, under review here, is devoted to the assessment of cancer risk for man from a knowledge of mechanisms and laboratory studies.

The book unfortunately disappoints in that it clearly shows that human risk assessment at the present time is difficult if not impossible. Several speakers discuss the severe limitations of carcinogenicity tests in animals. The recently developed short-term tests for carcinogens are little better as quantitative predictors. These tests, which depend on the fact that the majority of known carcinogens are DNA damaging agents either directly or after metabolic activation, have resulted in a breakthrough in our ability to detect potentially hazardous chemicals in the environment and their use is well documented by several authors. Some, however, would go further and suggest that a quantitative correlation may exist between mutagenicity for bacteria and carcinogenicity for mammals. As recent correspondence in the pages of *Nature* testifies, it will be no easy matter to convince toxicologists that this correlation is anything more than a crude approximation, if indeed it exists at all in a quantitative form. Nevertheless it is right that it should be studied since it may lead in time to more realistic ways of assessing risk.

The difficulties currently faced by regulatory authorities are clearly shown in the transcripts of three public policy panels in which the Food and Drug Administration and the Environmental Protection Agency defended their controversial handling of diethylstilboestrol, cyclamates and dieldrin, all suspected of presenting a human risk at current usage levels.

Although most human carcinogens are DNA damaging agents it is by no means established that the major environmental factors leading to cancer are actually carcinogens of this type, as is pointed out in a first rate paper by Peto. Indeed resolution of this problem is one of the most important tasks confronting us in preventive cancer research. In contrast to that by Peto, most papers in this book could be described as being low on thought and amounting to little more than restatements of already well known positions. It is time that the profession got to grips with the problem of carcinogenic risk assessment. It is a task that will need co-operation between the epidemiologist and the laboratory worker, for neither is likely to succeed in isolation.

B. A. BRIDGES.

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Computers in the Control of Treatments Units

The British Institute of Radiology: Special Report No 16, March 1979

by R. E. Bentley, A. L. Bradshaw, C. A. F. Joslin, W. J. Redmond, M. E. Rosenbloom, B. J. Scholl-Evans, J. B. H. Stedeford and R. C. Tudway.

Digital computers are being used very successfully in radiotherapy dose computation. This report deals with another, at present less highly developed, application of computers, the provision of some degree of automation at the point of treatment. Drawing on their own practical experience, on information from manufacturers and on the relatively sparse literature on this topic, the authors analyse the reasons for wishing to introduce some automation, discuss suitable techniques and procedures and make specific recommendations. Practical problems in implementing such control systems, including the need to gain acceptance from those operating the equipment and from those being treated, are carefully considered.

The authors were of a multidisciplinary Task Group, convened by Dr. Roy Bentley, which had been set up by the British Institute of Radiology Working Party on "Applications of Modern Technology in Radiotherapy."

The report should be of interest to all those concerned as users, designers or manufacturers with future developments of radiotherapy apparatus.

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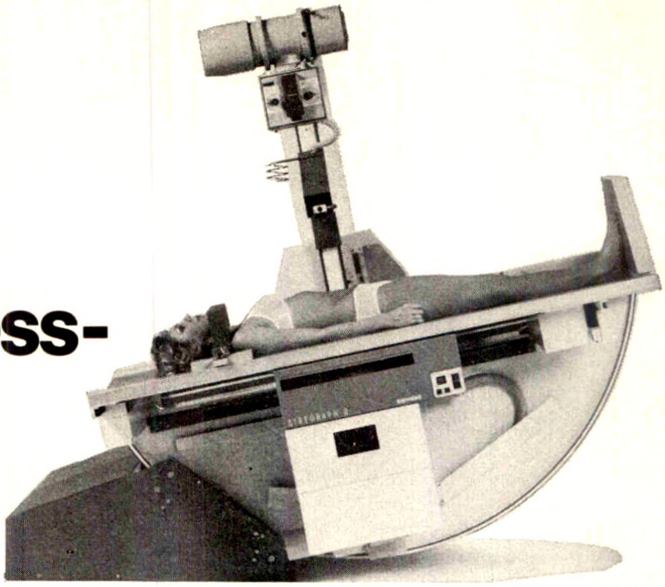

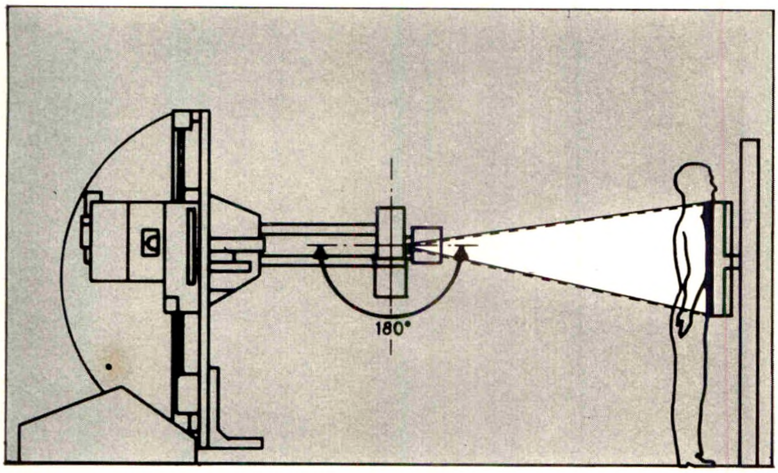

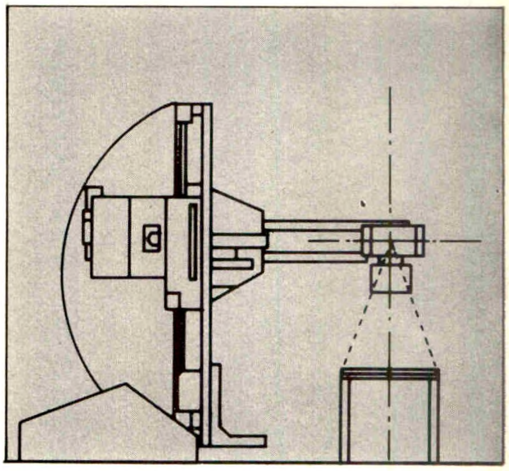

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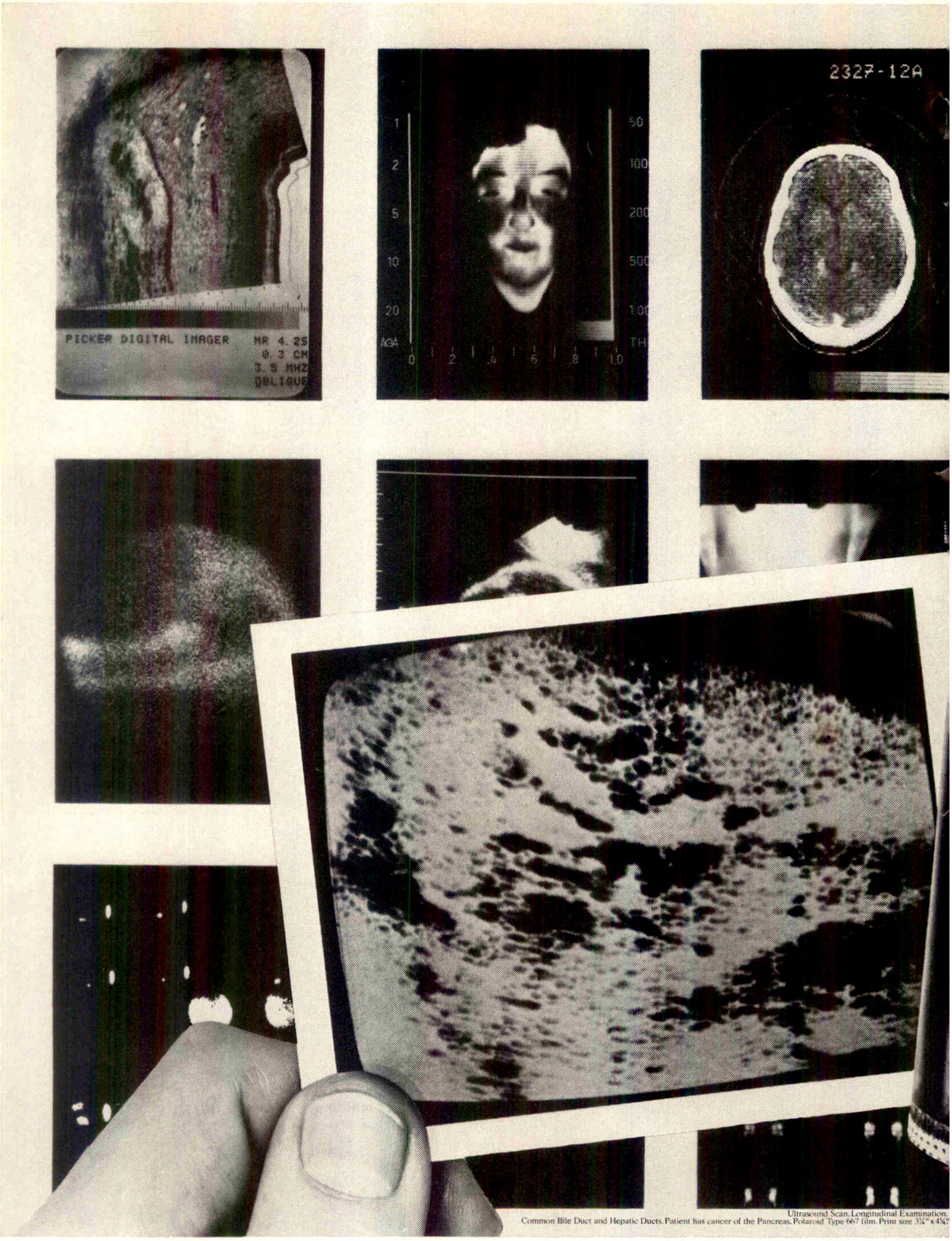

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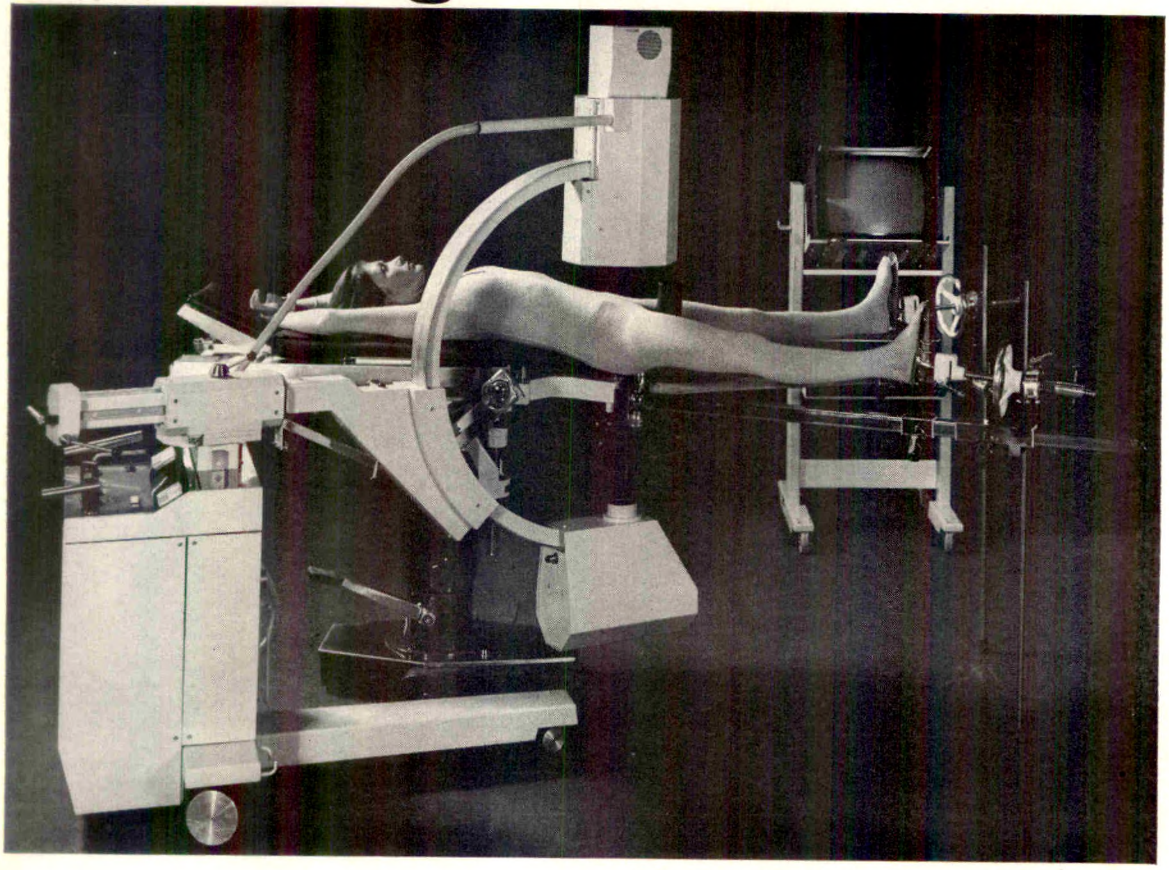

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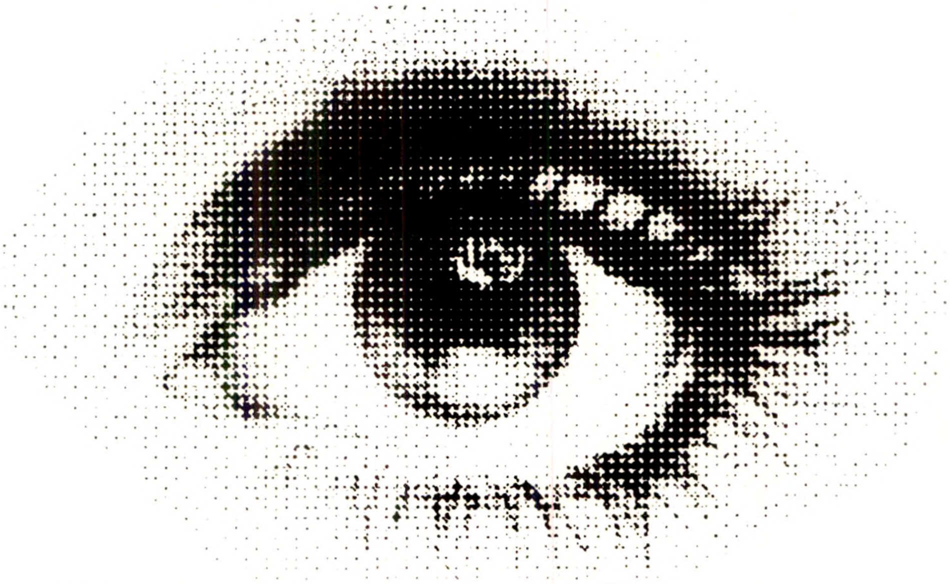

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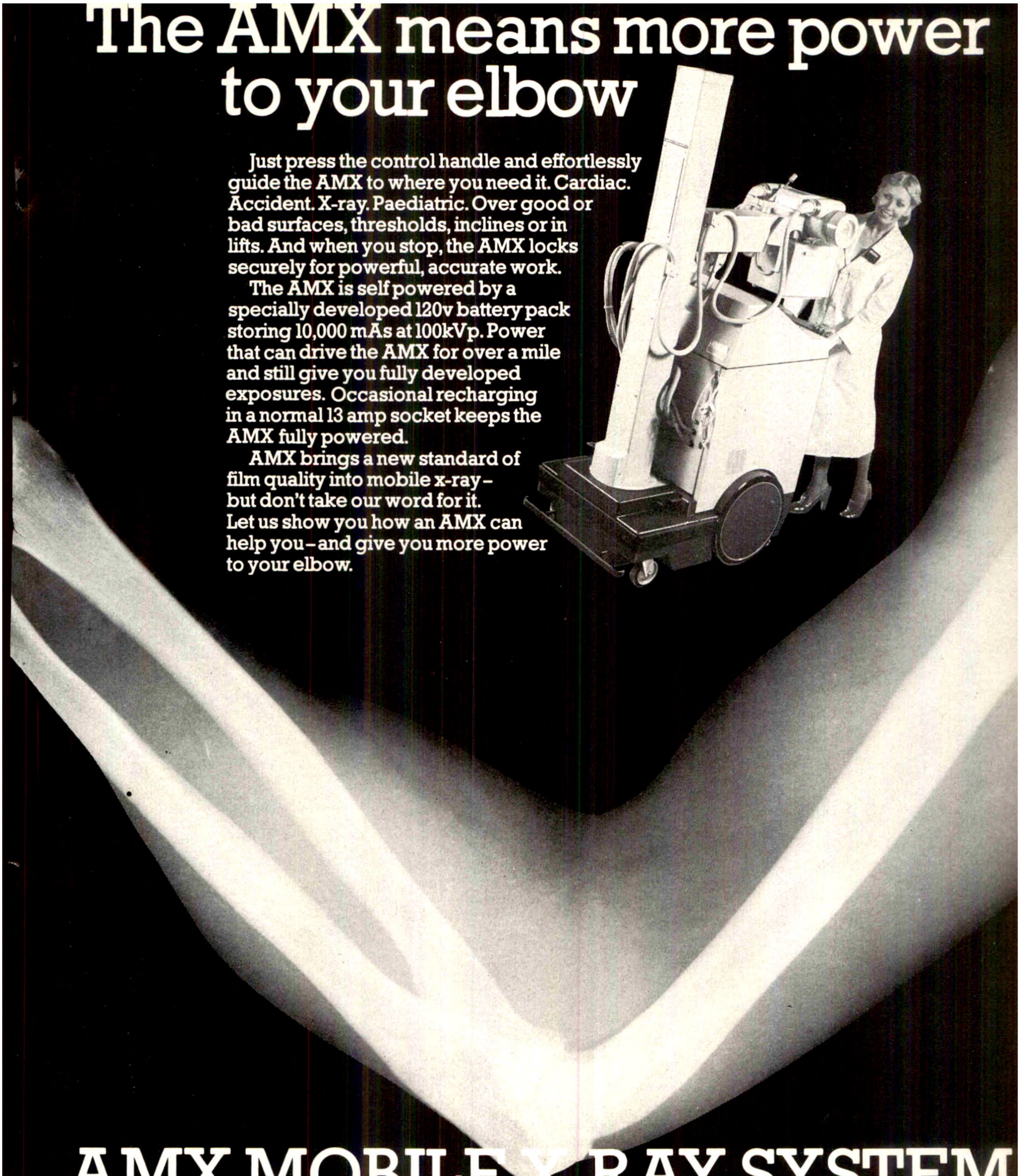

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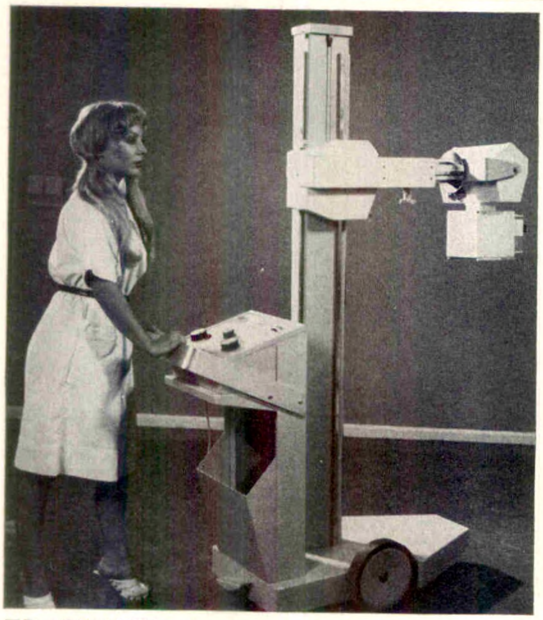

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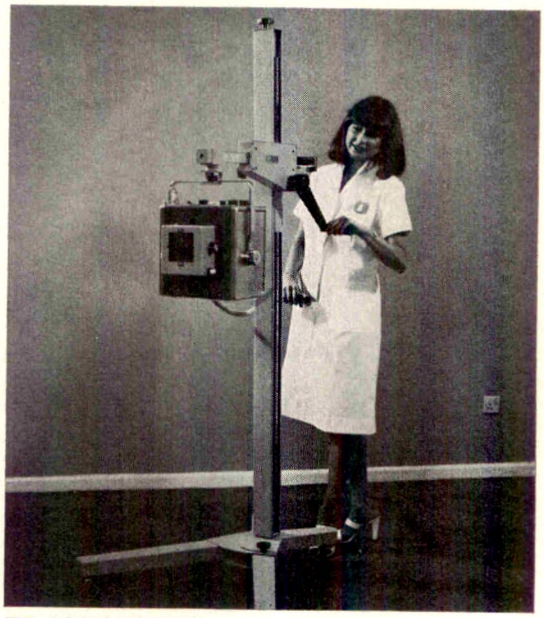

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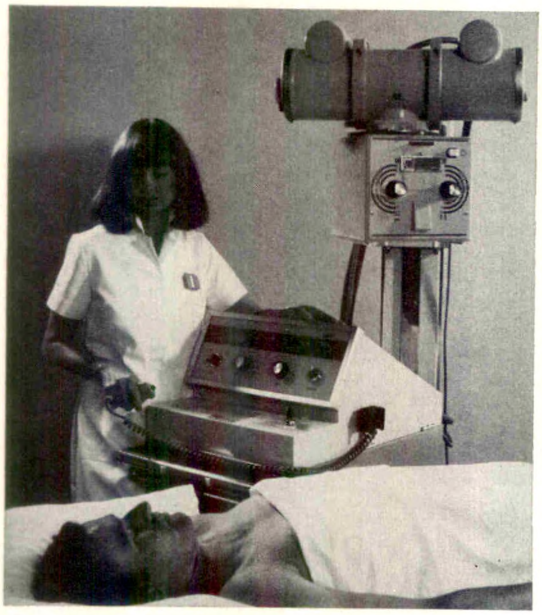

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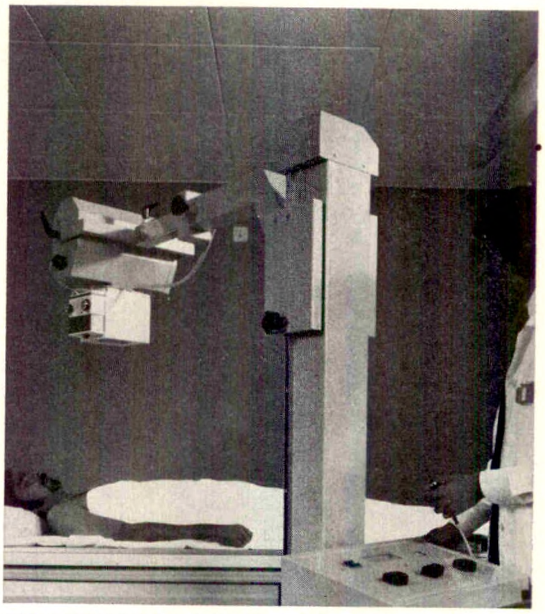

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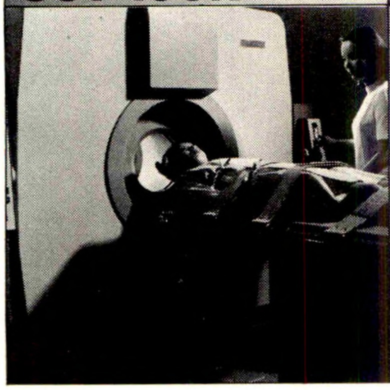

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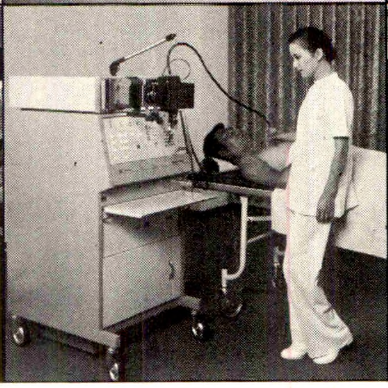

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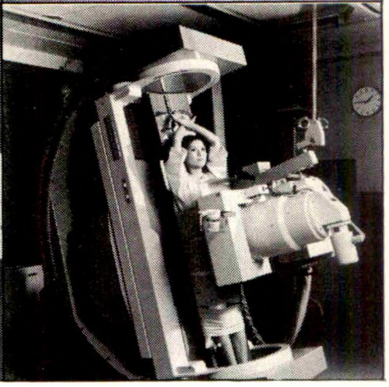

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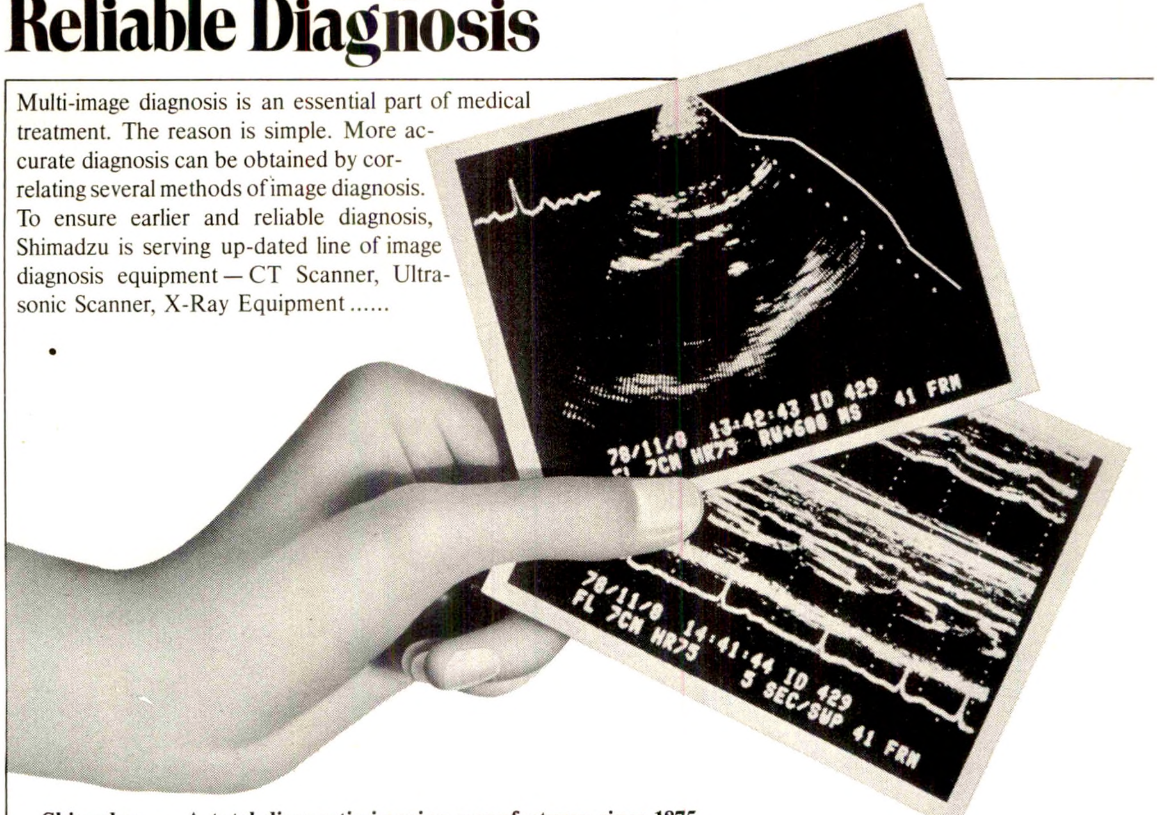

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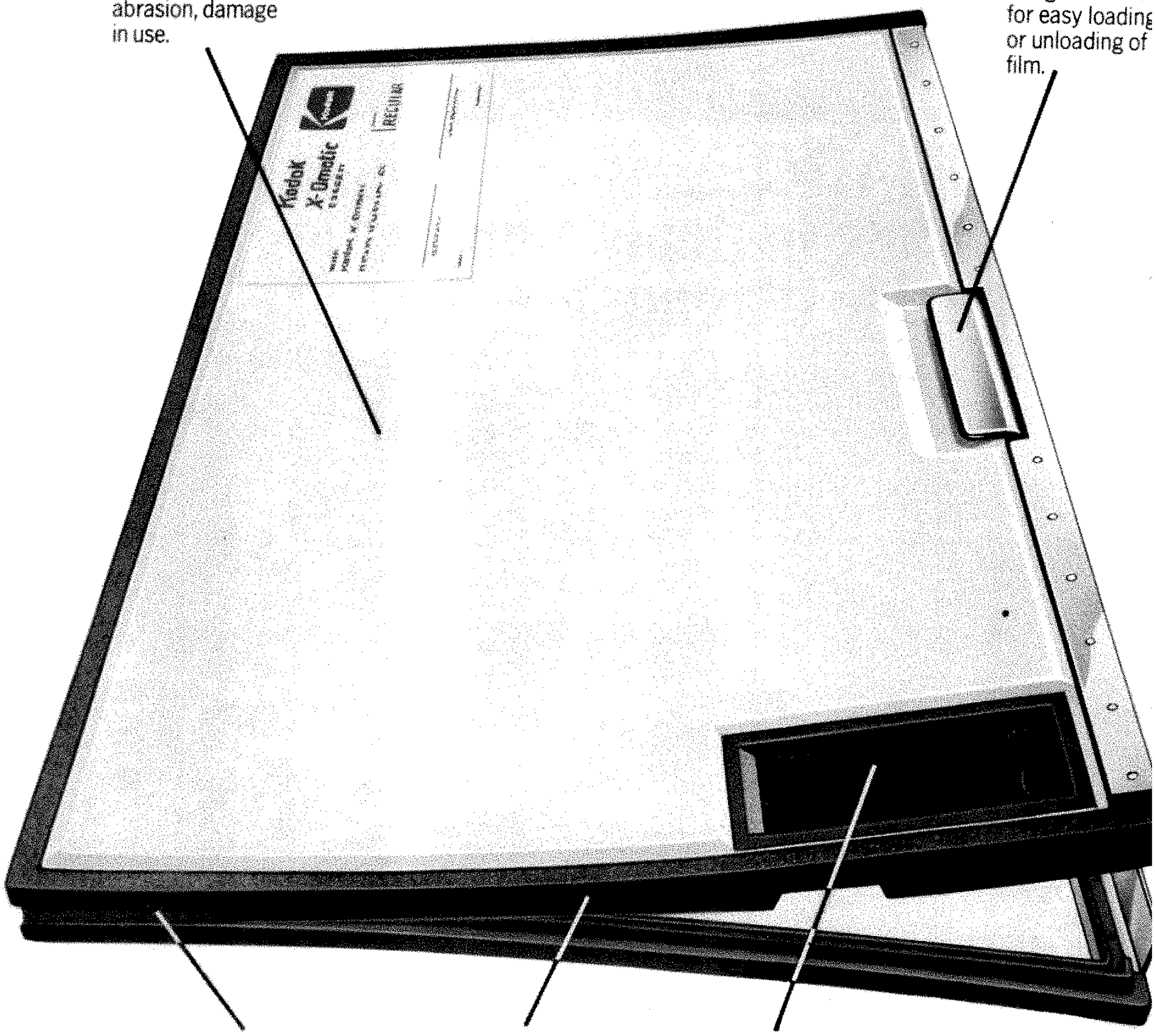

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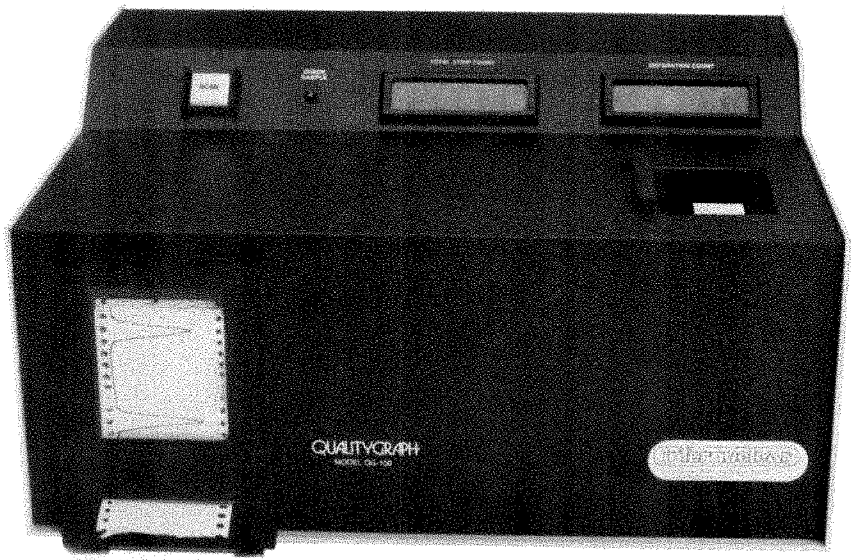

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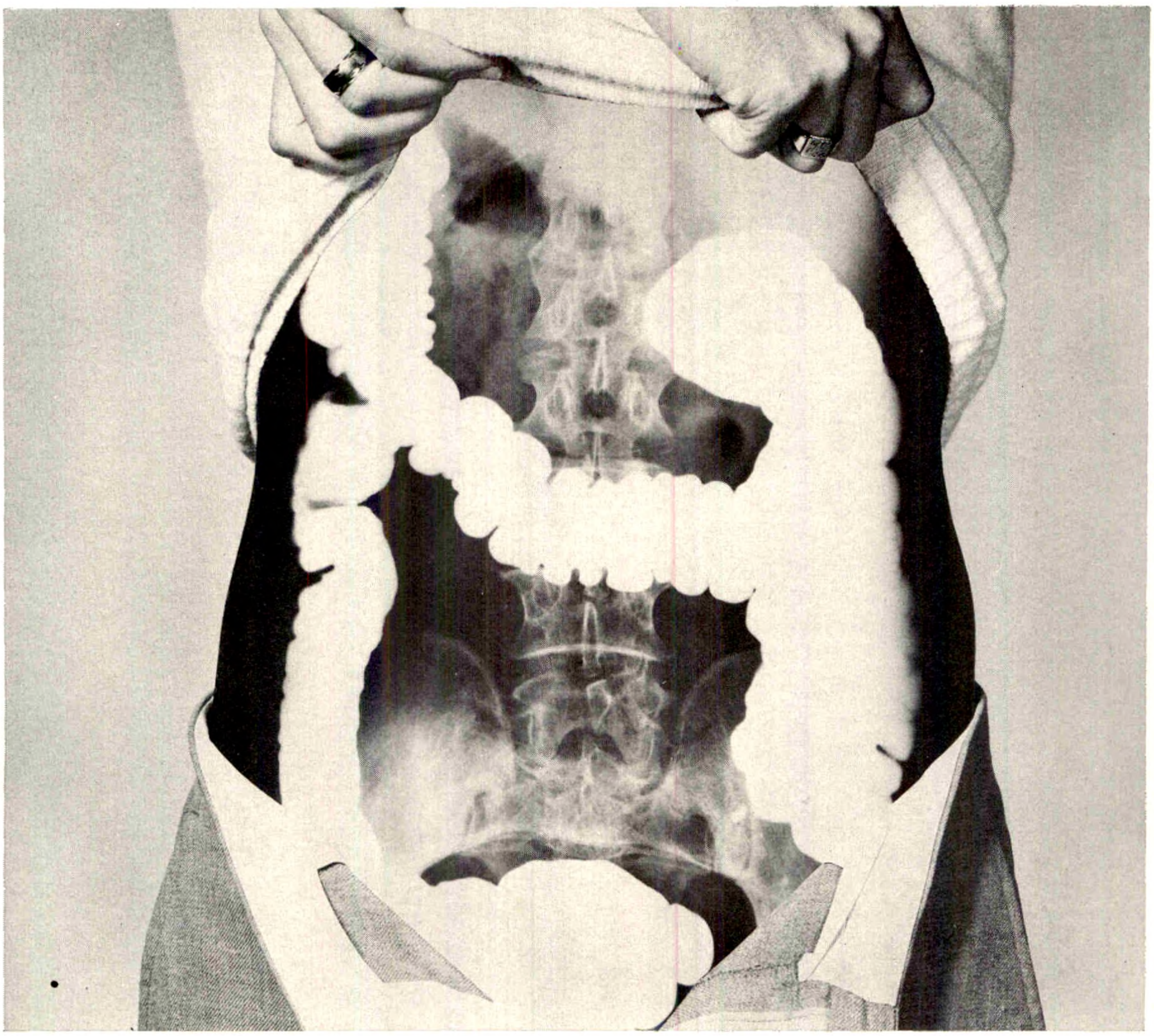

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1979. 183 figures. Approx. 432 pages
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Contents:
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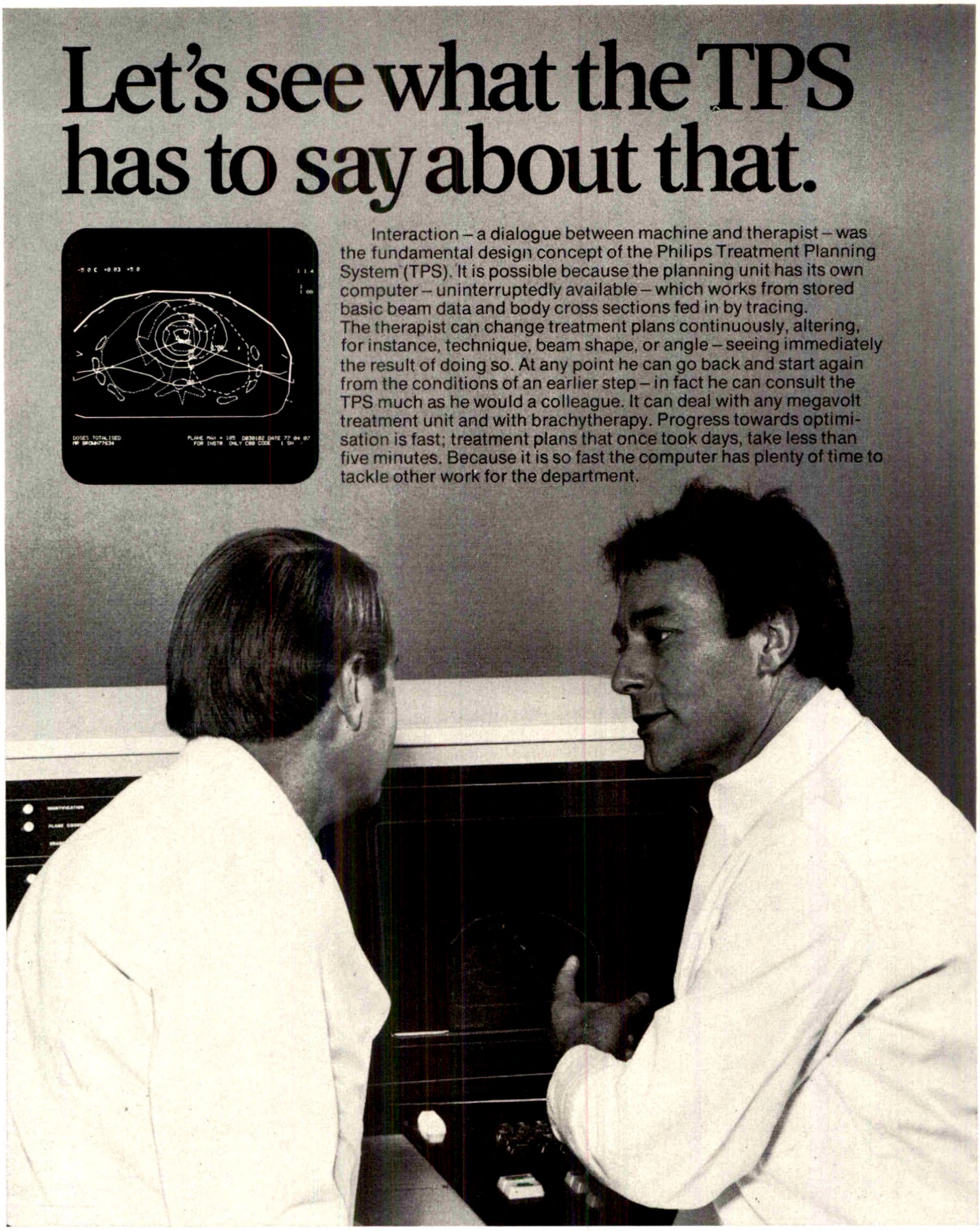

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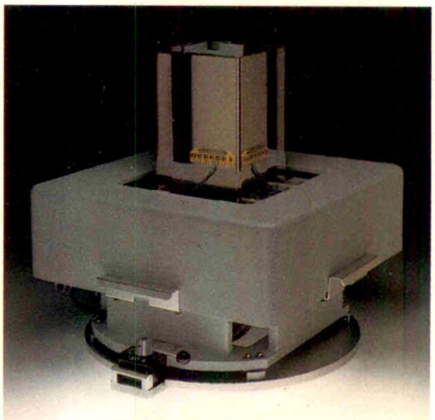

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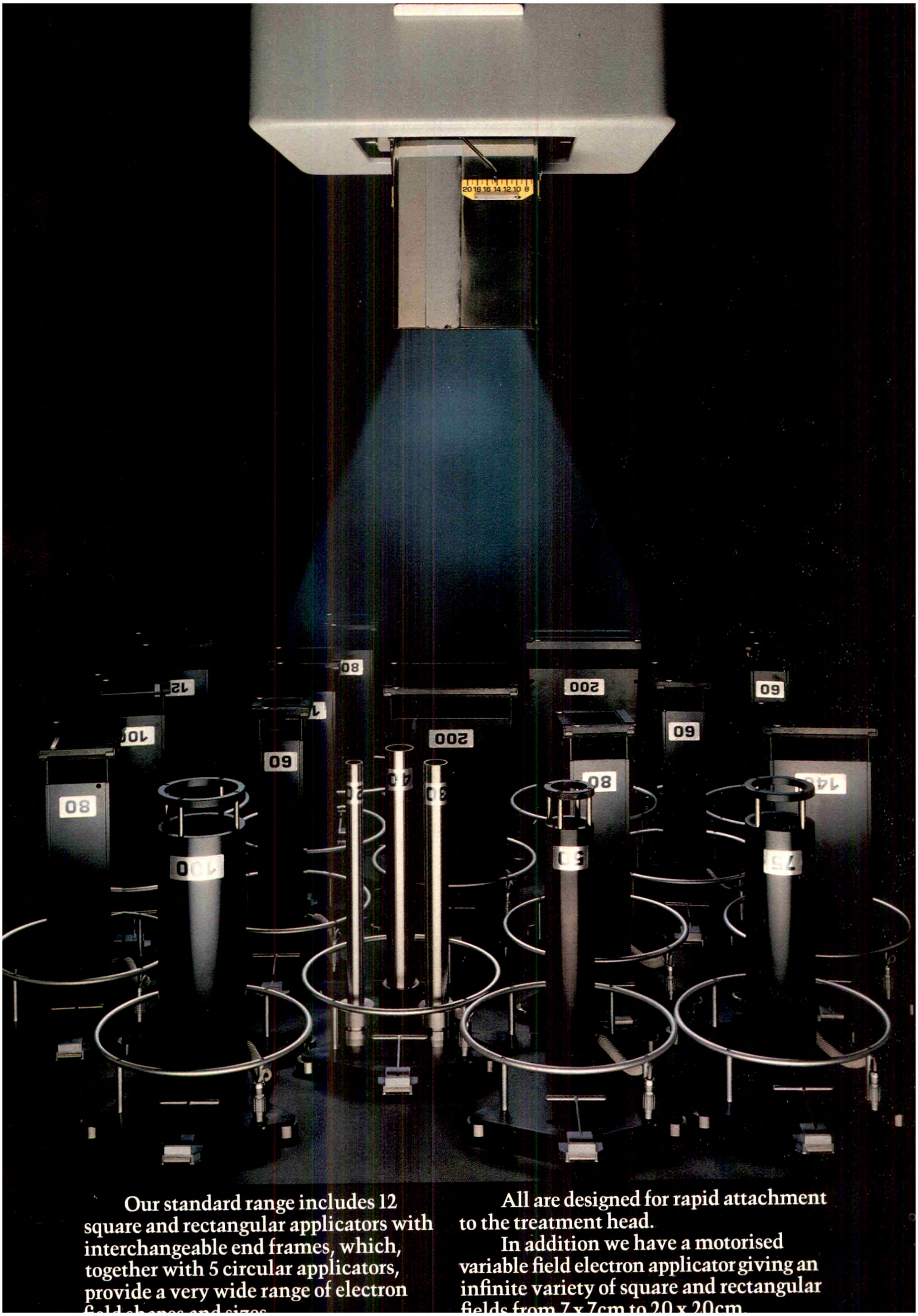

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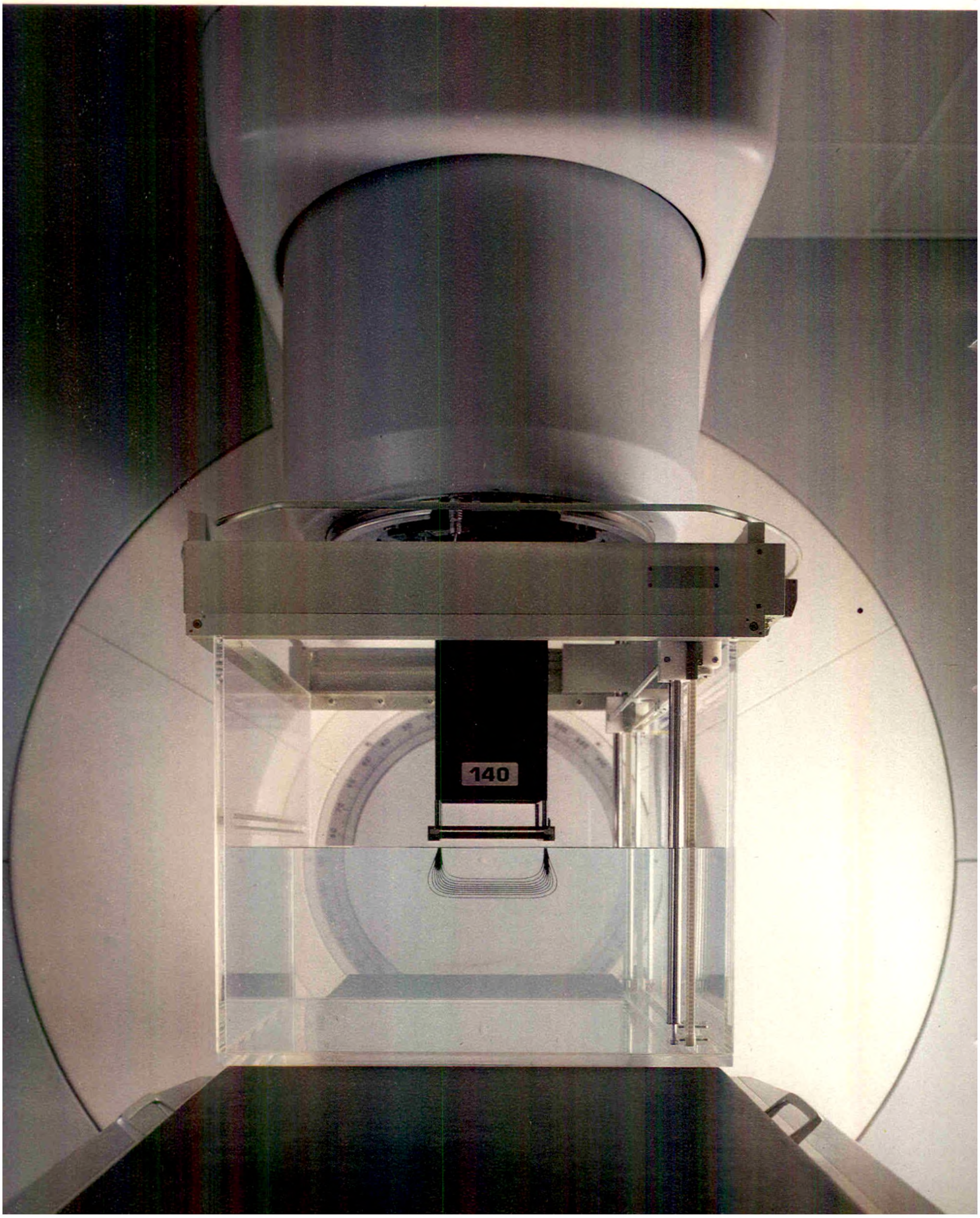

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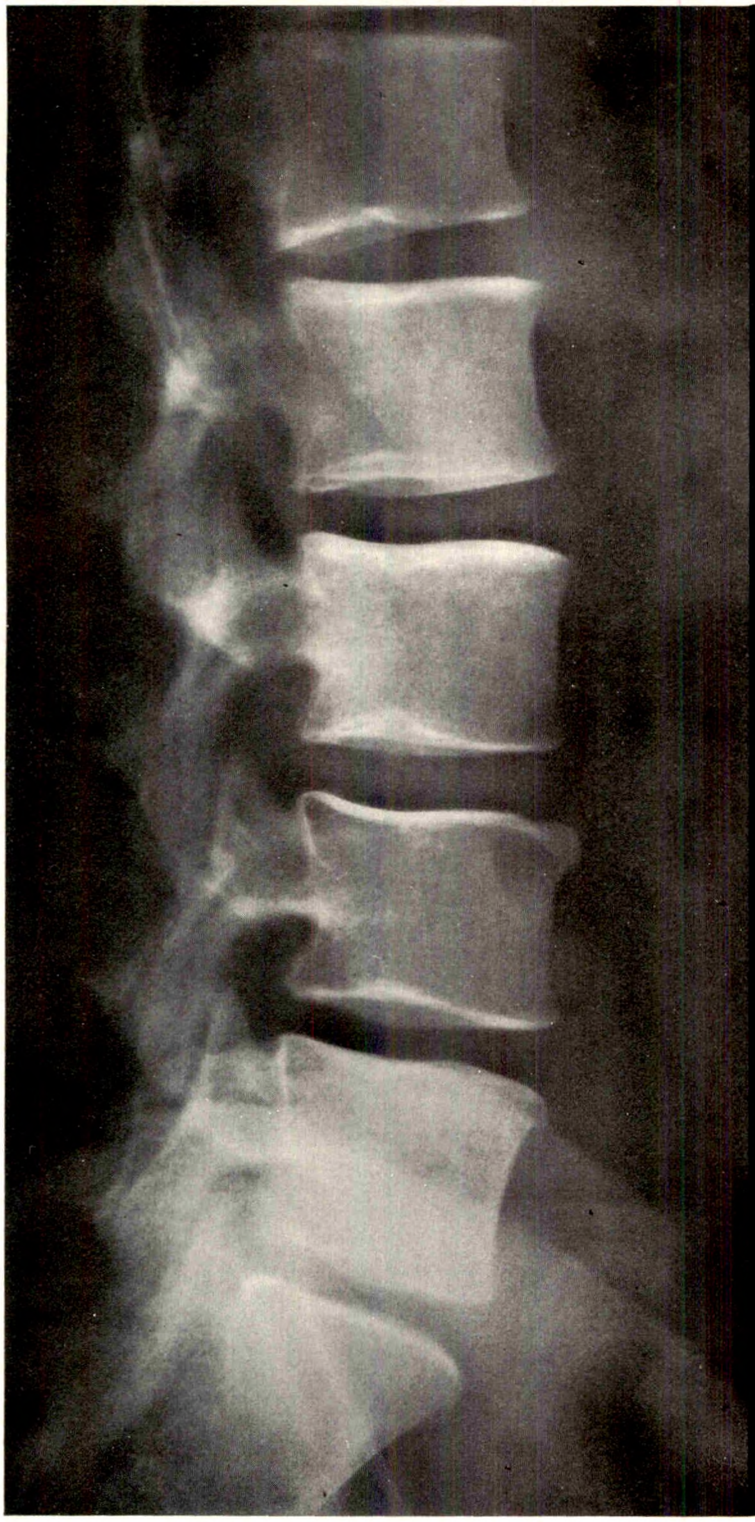

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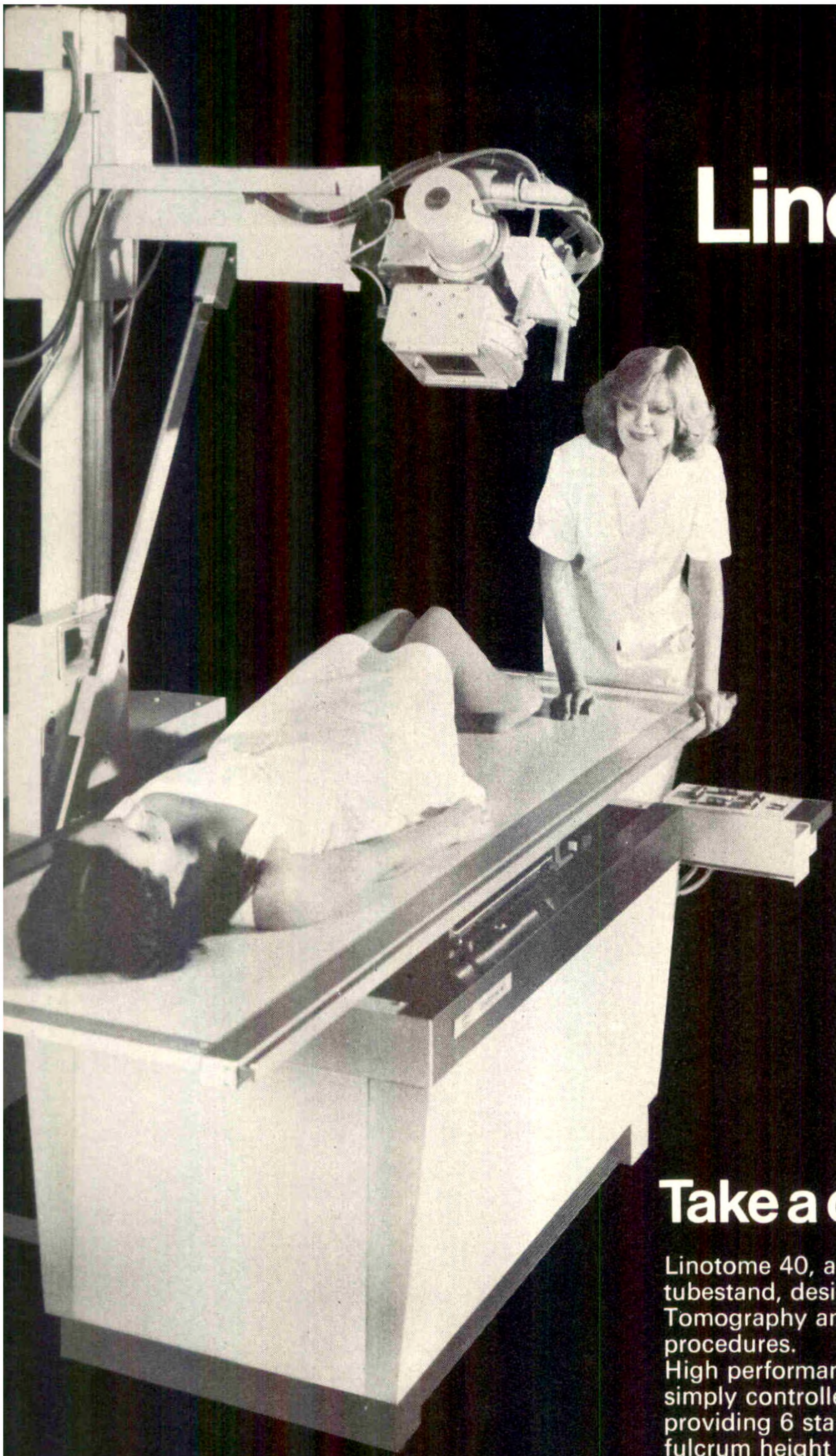

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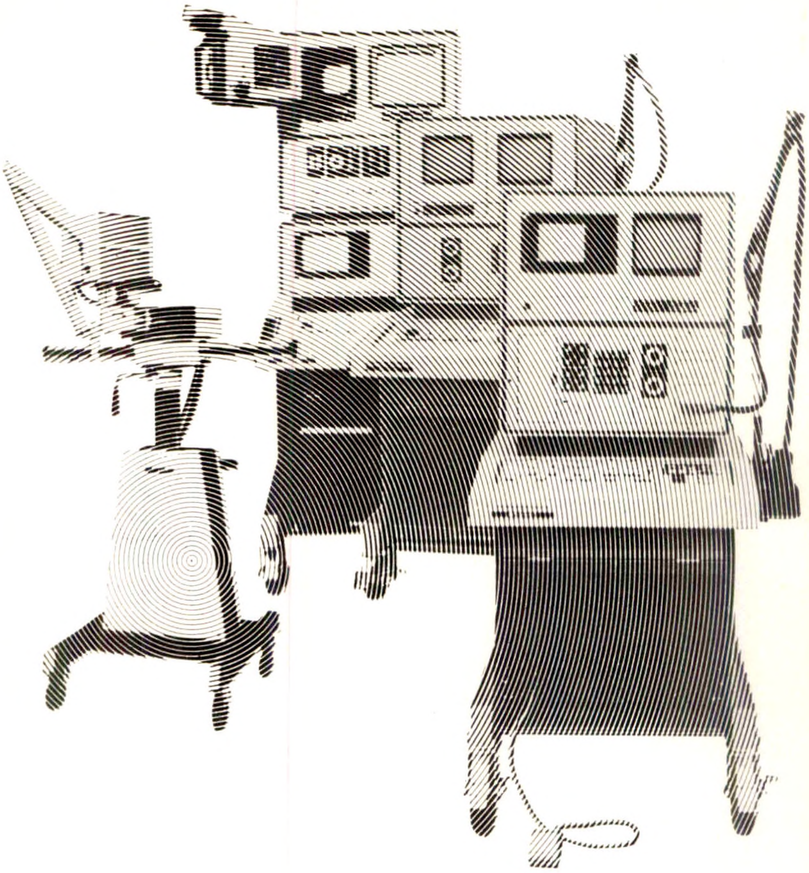

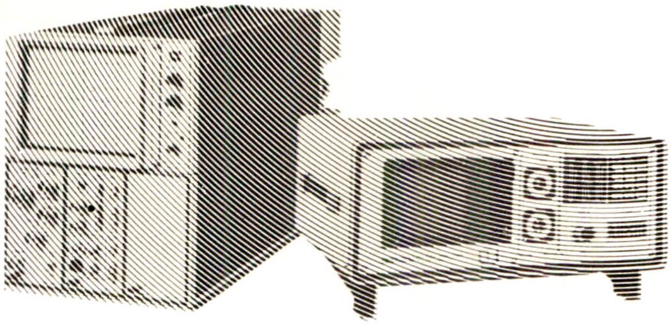

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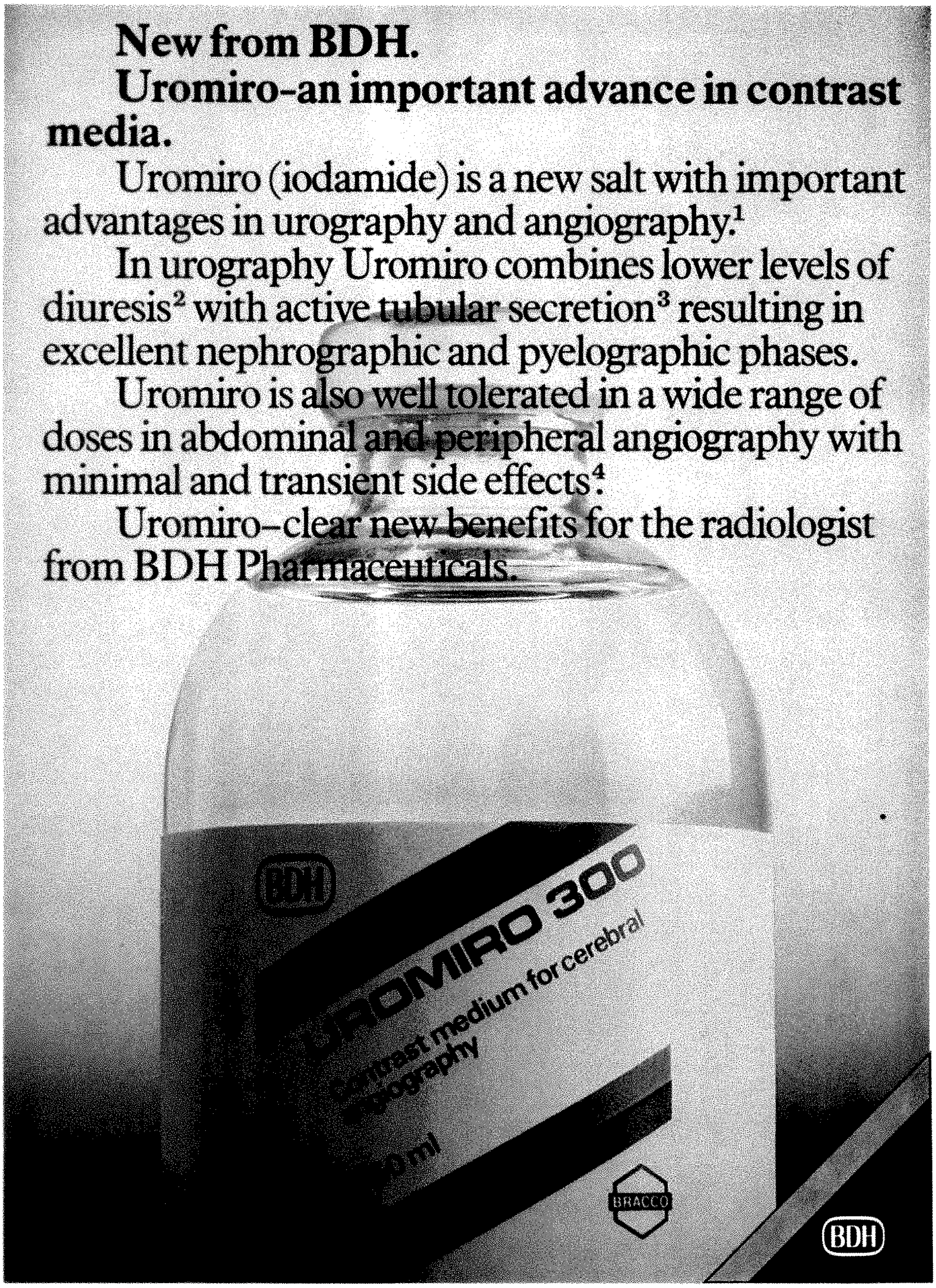

References 1. Bonati et al, (1965) Arzneimittel-Forschung, 15, 222-229. 2. Bellizi, (1966) Radiologica Radioterapia and Fisica Medica, 21, 3. 3. Bollerup et al, (1975) European Journal of Clinical Pharmacology, 9, 63-67 4. Kaude, (1973) Der Radiologe, 13, 271-275

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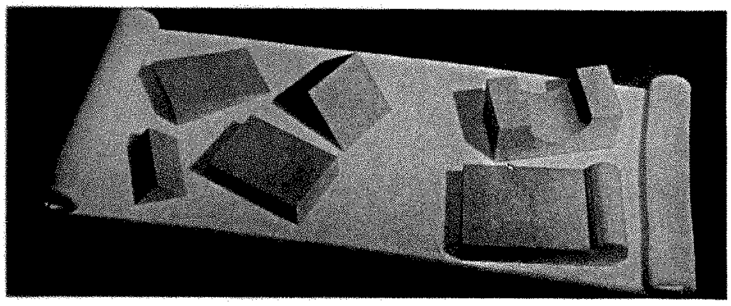

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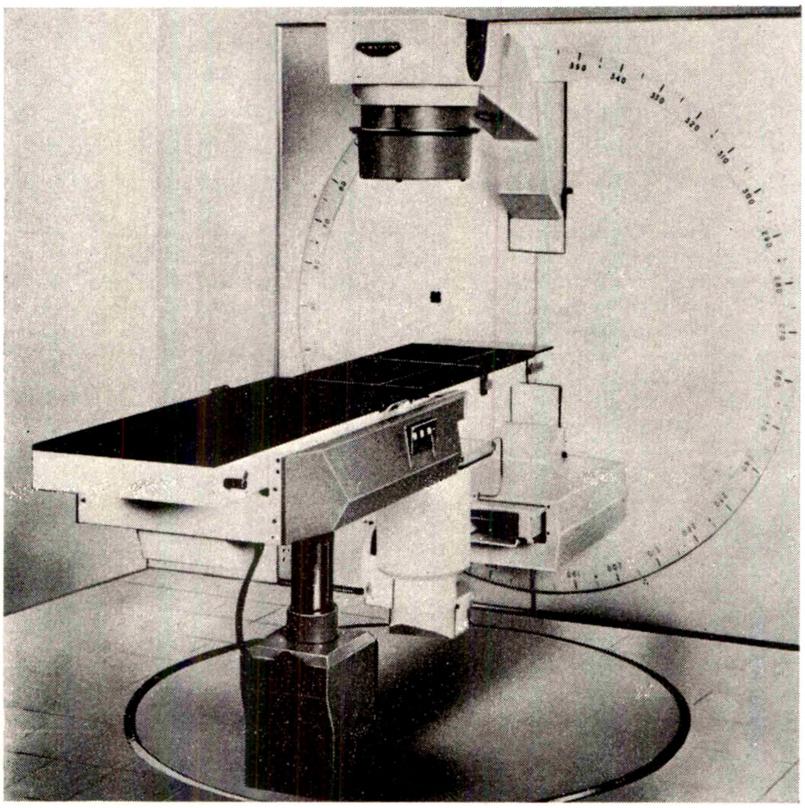

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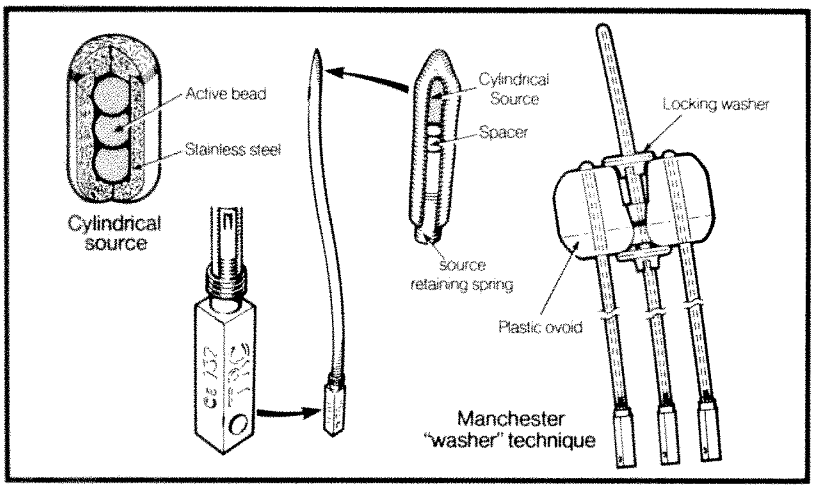

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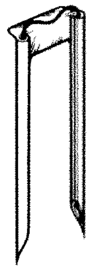

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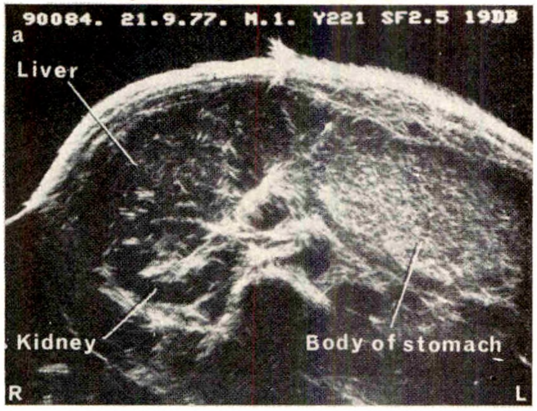

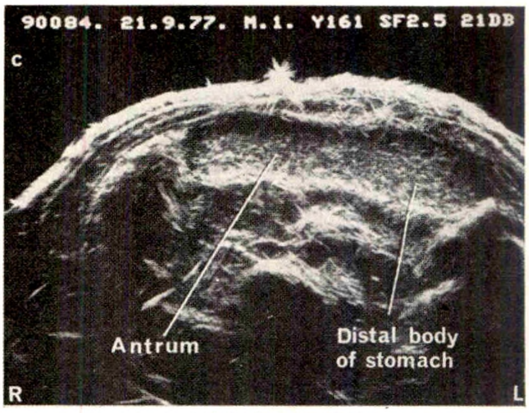

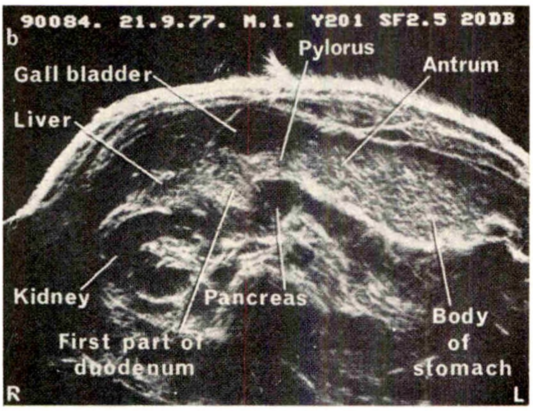

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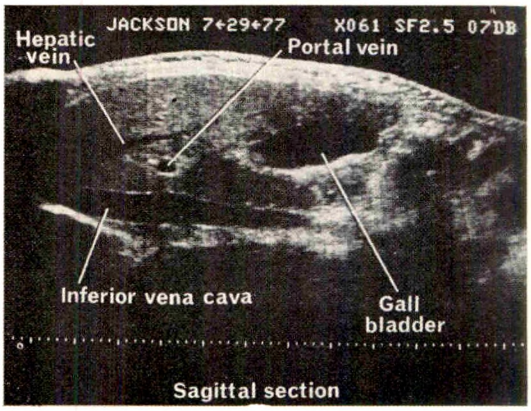

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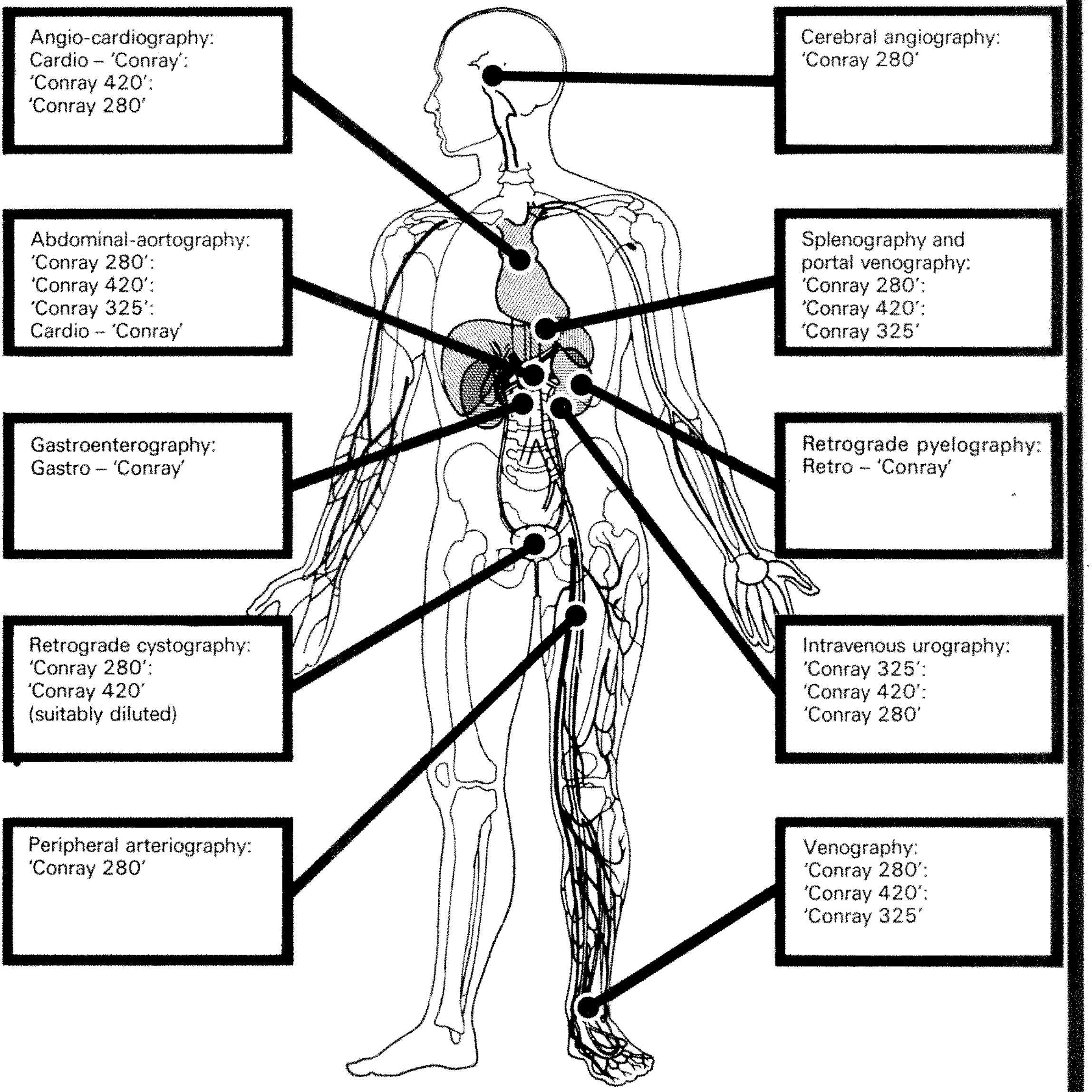

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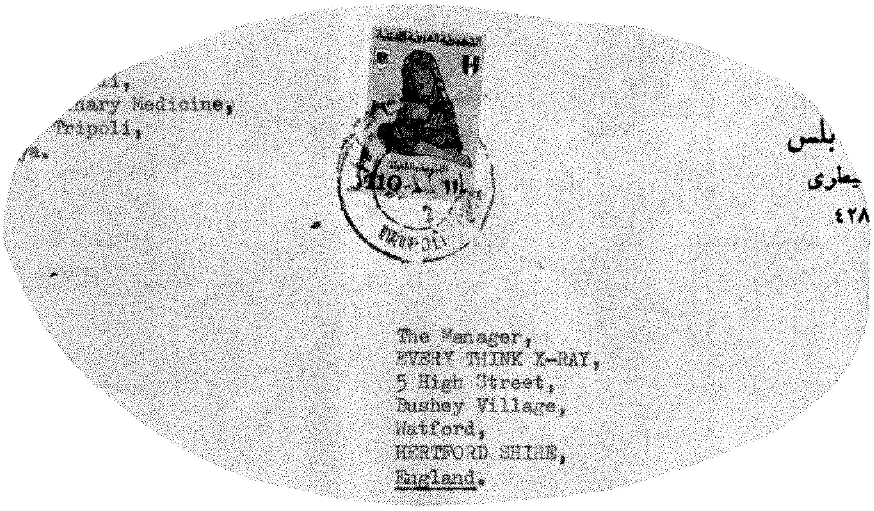

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The radiological manifestations of metaphyseal dysplasia (Pyle disease)

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ABSTRACT

Pyle disease is a rare genetic skeletal disorder which is conventionally classified with craniotubular dysplasias. The radiographic manifestations in three affected adults included widening of the metaphyseal portions of the long bones which extended through a major portion of the diaphyses, with cortical thinning and mild cranial sclerosis. The femora presented the characteristic Erlenmeyer flask configuration.

Pyle disease is clinically, radiographically and genetically distinct from craniometaphyseal dysplasia, a relatively common condition with which it has been confused.

Metaphyseal dysplasia or Pyle disease is an extremely uncommon bone disease in which gross abnormalities of tubular bone modelling are associated with mild sclerosis of the cranium. Prominent radiographic features in the long tubular bones consist of splaying of the metaphyses with relative constriction of the diaphyses. The changes are most obvious in the lower femora, where the appearance has been likened to an "Erlenmeyer flask". Failure of modelling may also be seen in the short tubular bones and there is widening of the medial ends of clavicles, sternal ends of ribs and pubic bones. In spite of the striking radiographic manifestations there are few clinical stigmata and the condition has a benign course.

Following the initial description by Pyle (1931) of a five-year-old boy with "unusual bone development", about 20 genuine cases have been reported. There has been considerable semantic confusion with craniometaphyseal dysplasia which is far more common, and a number of mis-diagnoses have occurred. As these conditions differ in their course and prognosis, diagnostic accuracy is important. In order to draw attention to this situation, we depict and discuss the radiological features of three adults with Pyle disease.

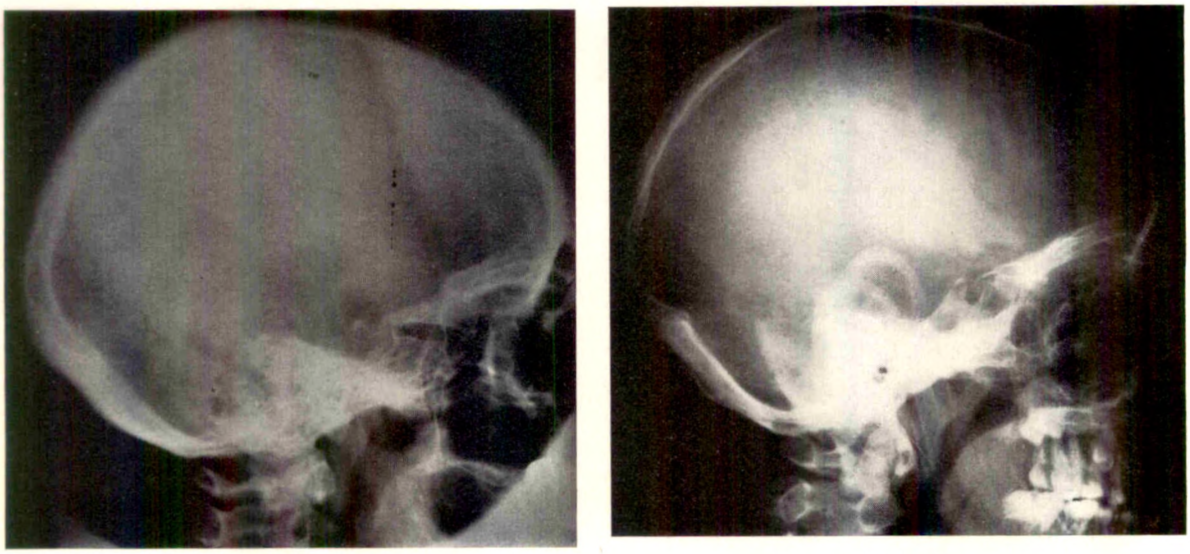
PATIENTS AND METHODS

During the period 1970–1978, 80 individuals with genetic conditions in which cranial sclerosis or abnormal modelling of the appendicular skeleton were major features, have been encountered in our skeletal dysplasia clinics. Of these, three were suffering from Pyle disease while the others had diverse disorders, including osteopetrosis, sclerosteosis and craniometaphyseal dysplasia.

Two of our patients with Pyle disease were members of a large consanguineous Afrikaner kindred. Patient 1, a 24-year-old female, was asymptomatic and the disorder was only recognized during adolescence following wrist injury. A subsequent skeletal survey revealed typical changes of Pyle disease and numerous old healed fractures. Radiological examination of family members revealed almost identical changes in a male cousin aged 20 years (patient 2). Genu valgum and palpably widened metaphyses in the long bones and clavicles were noteworthy clinical findings in both patients. Patient 1 was edentulous while patient 2 manifested carious teeth and dental malocclusion.

In addition, the radiological study of the kindred revealed mild undertubulation of the femora in seven obligatory or potential carriers of the abnormal gene. The genetic implications of these findings have been considered elsewhere (Raad and Beighton, 1978).

Patient 3, a 50-year-old Afrikaner male, was investigated radiologically following low back pain. Radiographs revealed a lumbosacral spondylolisthesis and mild platyspondyly. Gross metaphyseal flaring was evident on skeletal survey for suspected



A *Patient 1.*

B *Patient 2.*

skeletal dysplasia. Corresponding widening of the metaphyses in the long bones and clavicles was clinically evident.

RADIOGRAPHIC FINDINGS

Axial skeleton

Skull

Patchy sclerosis was present in the calvarium and base in all three patients and each had moderate supra-orbital prominence. The paranasal sinuses and mastoid air cells showed partial or complete non-pneumatization. Prognathism was evident in all three patients. Patients 1 and 3 were edentulous (Fig. 1).

Thorax

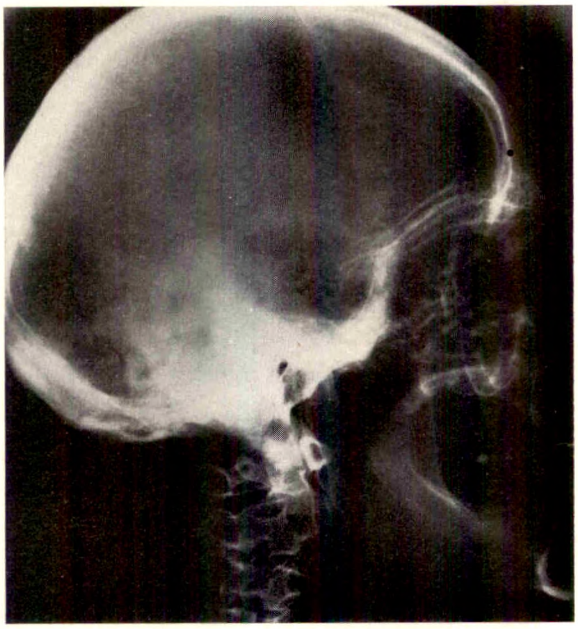
All three patients exhibited striking modelling abnormalities in the clavicles and to a lesser degree in the ribs. Flaring of the clavicle was most marked medially (Fig. 2) while the ribs were most flared at their costochrondral junctions. The scapulae were uninvolved and the heart and lungs were normal.

Spine

Spinal abnormalities were encountered in two of our patients. Patient 1 had a slight dorsal scoliosis (Fig. 3) while radiographs of patient 3 revealed a lumbosacral spondylolisthesis and mild platyspondyly in the dorsal spine (Fig. 4).

Pelvis

Abnormal widening of the ischio-pubic rami was a notable feature in each patient (Fig. 5). The configuration of the iliac crests was normal.



C *Patient 3.*

FIG. 1.

Skull. Patchy sclerosis of calvarium and base. Distinct supra-orbital bulge. Poor pneumatization of mastoid air cells and paranasal sinuses. Prognathism and widening of mandible.

Tubular bones

Upper limbs

Undertubulation of the humeri, which extended beyond the mid-diaphysis, was encountered in all our patients. This feature was most marked proximally and associated with cortical thinning (Fig. 6). Similar changes were present in the radii and ulnae, in which undertubulation was more pronounced distally (Fig. 7). In the short tubular bones of the hands the modelling defect occurred in the epiphyseal regions of the proximal ends of the phalanges, the first metacarpals and the distal ends of the other metacarpals.

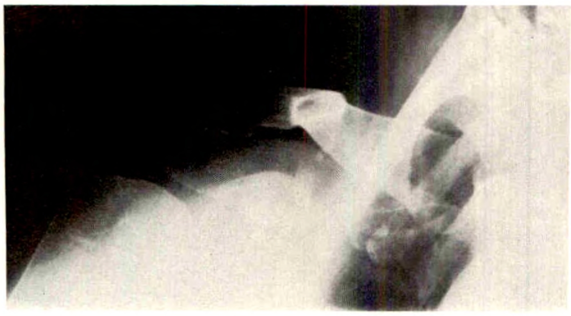
Numerous old healed fractures involving the metacarpals, phalanges and right radius in patient 1 (Fig. 8B) represent the sequelae of the underlying bone fragility in this patient, who had in addition radiographic evidence of fractures elsewhere in the skeleton.

Lower limbs

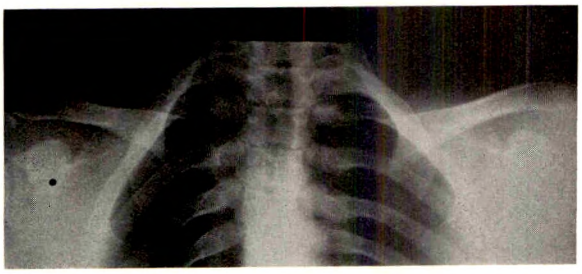
Modelling abnormalities were a dramatic feature in all three patients. As in the upper limbs cortical thinning and diminution of bone density was seen in the areas of maximal flaring.

In the femora the changes were most marked distally where gross "Erlenmeyer flask" deformities were evident (Fig. 9). This flaring extended proximal to the mid-femoral diaphysis where endosteal cortical thickening was present (Fig. 10).

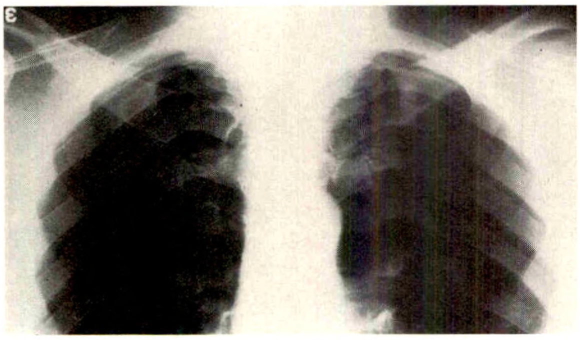
The tibiae and fibulae were expanded with mid-diaphyseal cortical thickening. Lateral bowing of the tibiae produced an S-shaped configuration (Fig. 11).



A *Patient 1.*



B *Patient 2.*



C *Patient 3.*

FIG. 2.

Clavicles. Clavicles markedly flared medially. Ribs widened to a lesser degree.

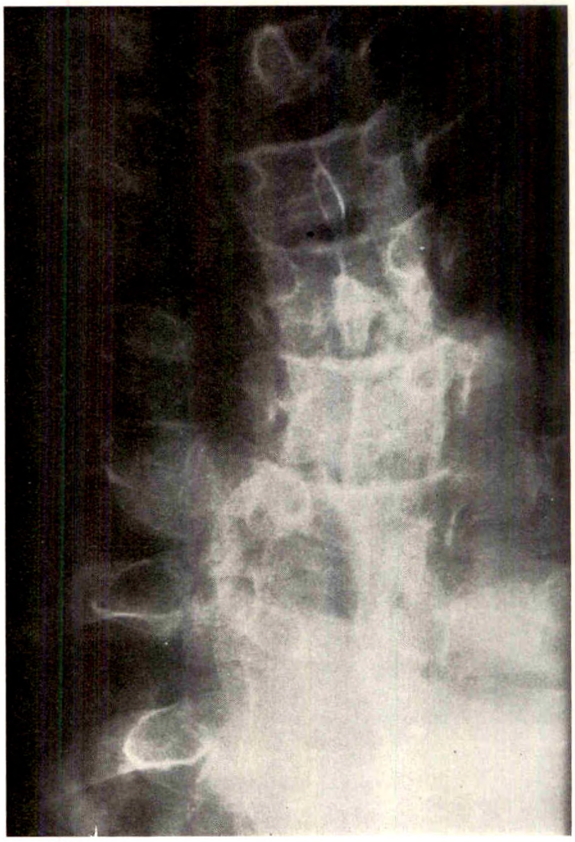


FIG. 3. *Patient 1.*

Mild dorsal scoliosis.

N. G. Heselson, M. S. Raad, H. Hamersma, B. J. Cremin and P. Beighton

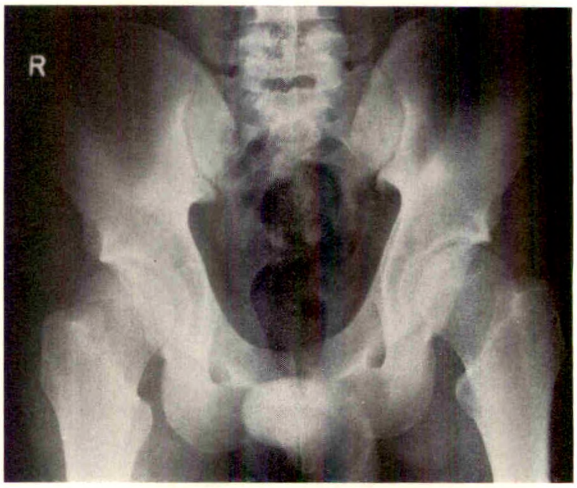


FIG. 5. *Patient 2.*
Widening of ischio-pubic rami.

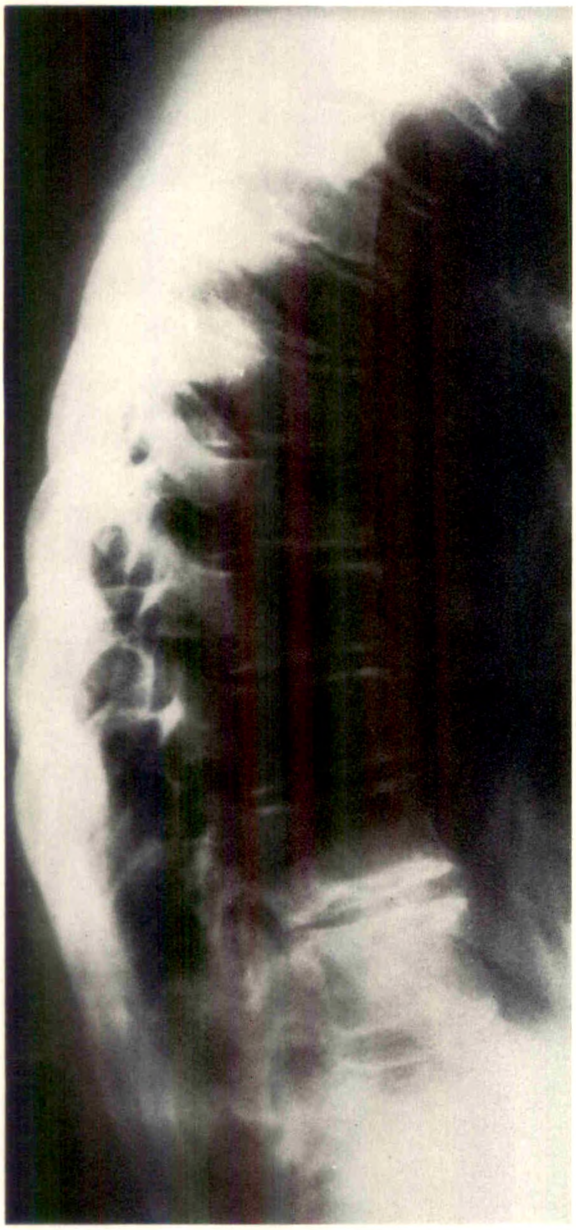


FIG. 4. *Patient 3.*
Mild dorsal platyspondyly.

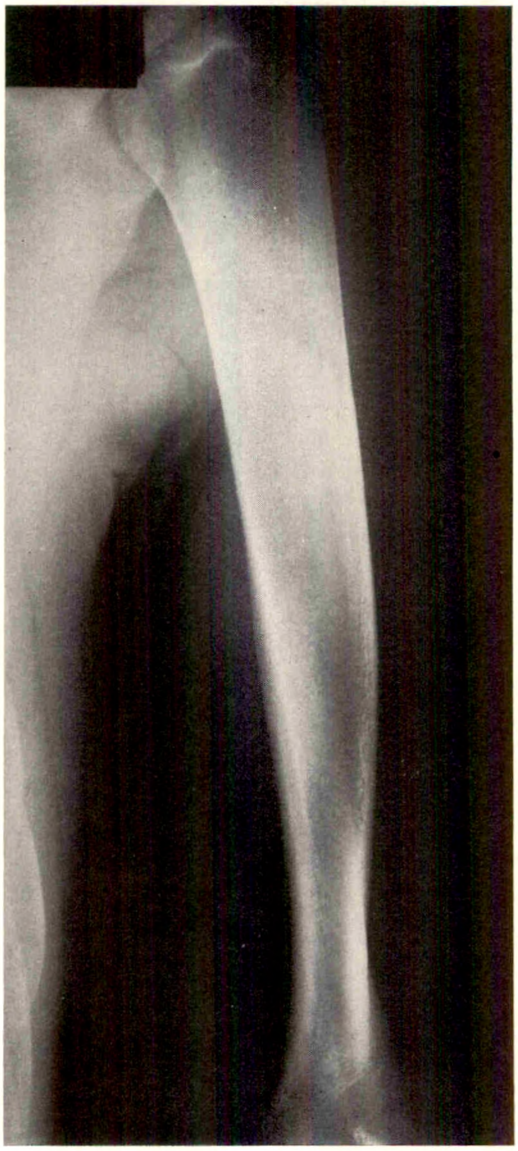
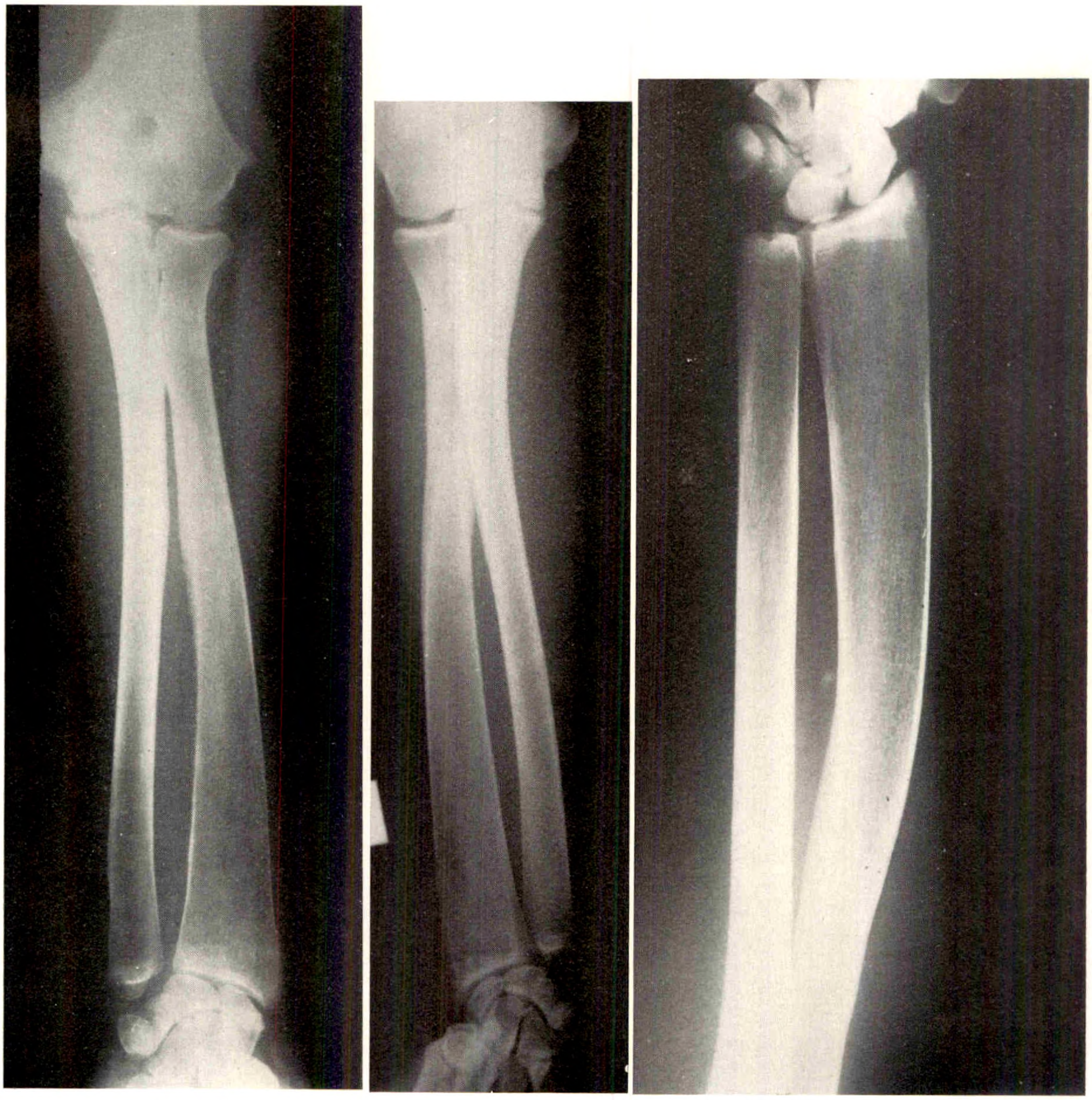


FIG. 6. *Patient 1.*
Undertubulation of humerus in its proximal two-thirds.

Radiographs of seven obligatory and potential heterozygotes in the family of patients 1 and 2 revealed mild but definite undertubulation of their distal femora (Fig. 12).

DISCUSSION

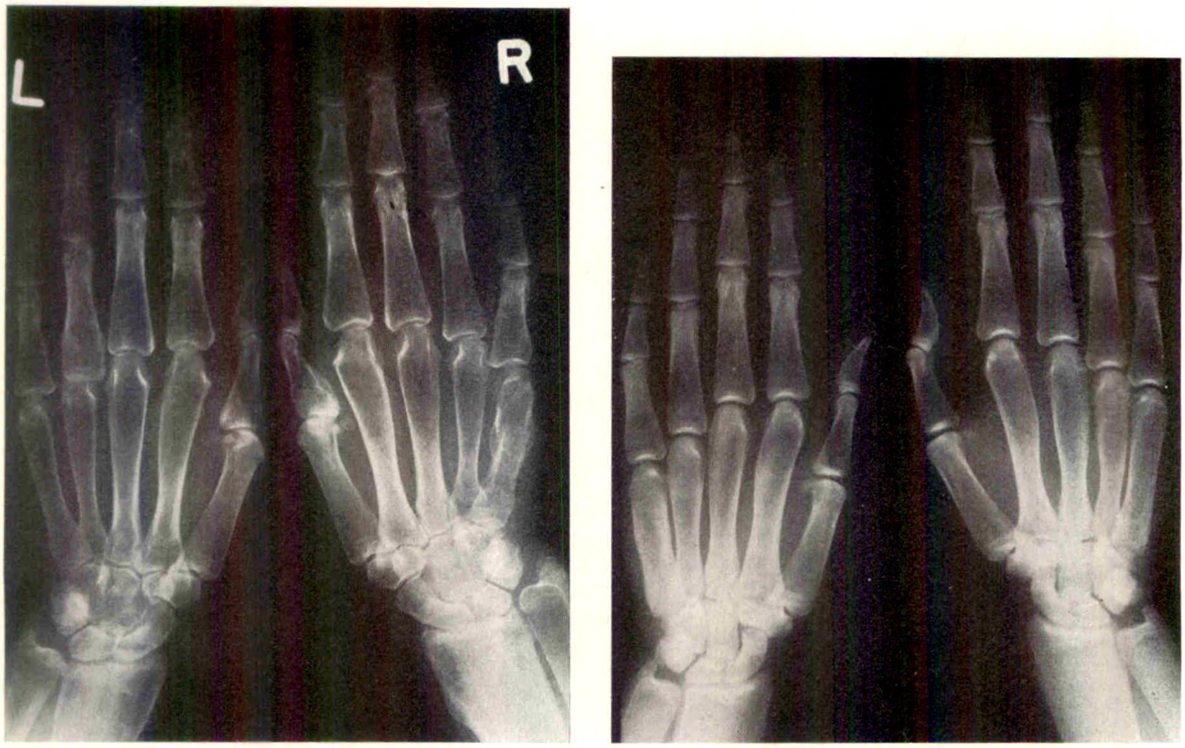
Pyle disease is a rare disorder in which striking radiographic manifestations contrast with the relatively normal clinical features. The face and habitus are unremarkable and genu valgum, as seen in all our patients, is the only consistent abnormality. Bone fragility, as in case 1, and spinal malalignment, as in cases 2 and 3, are infrequent but well documented complications (Pyle, 1931; Bakwin and Krida, 1937;



A *Patient 1.* B *Patient 2.* C *Patient 3.*

FIG. 7.

Undertubulation of radius and ulna in the distal two-thirds.



A *Patient 1.* B *Patient 2.*

FIG. 8.

Metacarpals 2–5 undermodelled distally, first proximally. Phalanges widened proximally. Note the old healed metacarpal, phalangeal and distal radial fractures in patient 1.

Hermel *et al.*, 1953). Carious and misplaced teeth, which either were or had been present in each of our patients, have been mentioned in several reports (Bakwin and Krida, 1937; Komins, 1954).

The radiographic changes which we observed were very similar to those described in an affected brother and sister by Feld *et al.* (1954). Patchy sclerosis of the cranial vault with associated moderate supra-orbital prominence, present in all of our three patients, are characteristic radiographic manifestations in Pyle disease (Gorlin *et al.*, 1969; Spranger *et al.*, 1974). Prognathism, a feature in all three of our patients is a common finding (Komins, 1954; Gorlin *et al.*, 1969; 1970).

Abnormal modelling (undertubulation) of the long and short tubular bones is the hallmark of metaphyseal dysplasia. The distal location of tubular bone expansion in the femora, radii, metacarpals and metatarsals; and the proximal location in the humeri, tibiae and phalanges of the hands and feet in all our patients is a typical finding (Hermel *et al.*, 1953; Gorlin *et al.*, 1969; Mabille *et al.*, 1973). Some reported patients were unusually tall (Pyle, 1931; Komins, 1954) but the majority have been of normal stature. In the two cases previously reported from South Africa (Komins, 1954), elongation of the big toe was a striking feature.

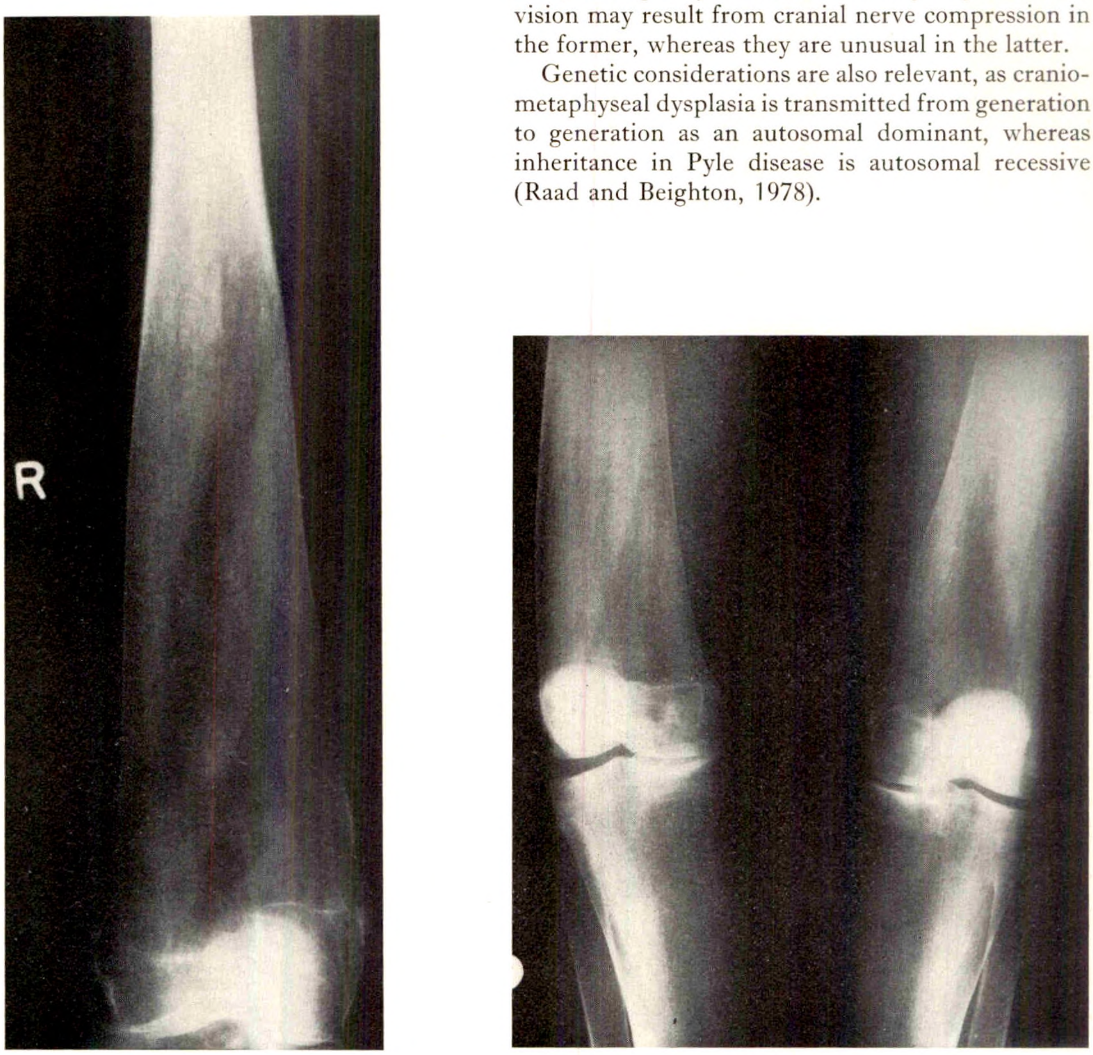
Thinning of the bone cortices in areas of abnormal bony expansion, as was evident in all our patients, and particularly noticeable in the distal femora and proximal tibiae, is an invariable accompaniment of bony expansion. Increased bone fragility is a well recognized but variable component of Pyle disease. In this context, the numerous old healed phalangeal, metacarpal and radial fractures evident in patient 1 represent the sequelae of increased bone fragility.

Evidence of previous bony injury was visible in other radiographs of this patient.

Scoliosis and platyspondyly present respectively in patients 2 and 3 are variable features (Gorlin *et al.*, 1969; 1970; Spranger *et al.*, 1974).

Since the original publication of Pyle (1931), other disorders characterized by abnormal bone modelling and varying degrees of skull sclerosis have been delineated. Prior to precise delineation of Pyle disease and craniometaphyseal dysplasia as separate entities many authors used these designations interchangeably (Mori and Holt, 1956; Walker, 1966; Holt, 1966; Ross and Altman, 1967). However, the two conditions are listed separately in the International Nomenclature of Constitutional Diseases of Bone (1969 and 1977). Gorlin *et al.* (1969) classified Pyle disease among the "craniotubulardys plasias" with craniometaphyseal dysplasia and rarities such as fronto-metaphyseal dysplasia, craniodiaphyseal dysplasia and dysosteosclerosis. Gorlin *et al.* (1970) and Mabille *et al.* (1973) emphasized that the distinction between craniometaphyseal dysplasia and Pyle disease is important in prognostication, since deafness, facial paralysis and occasionally impairment of vision may result from cranial nerve compression in the former, whereas they are unusual in the latter.

Genetic considerations are also relevant, as craniometaphyseal dysplasia is transmitted from generation to generation as an autosomal dominant, whereas inheritance in Pyle disease is autosomal recessive (Raad and Beighton, 1978).



A *Patient 1.* B *Patient 2.*

Fig. 9.

Femora exhibit gross "Erlenmeyer flask" deformities with marked cortical thinning and proximal extension.

Radiographic recognition of Pyle disease is not difficult, as the characteristic gross modelling defects of the long bones are not seen in any other condition. In particular, craniometaphyseal dysplasia is differentiated by the greater degree of cranial sclerosis and a "club-shaped" rather than an "Erlenmeyer flask" configuration of the distal femora. The "Erlenmeyer flask" deformity in Pyle disease has attracted the attention of many authors and Jackson *et al.* (1954) citing Hamman (1910) depicted a femur from a Nubian mummy in which this anomaly was present. However, the diagnosis of Pyle disease could not be firmly established in this particular instance as the femoral "Erlenmeyer flask" deformity may also be a manifestation of other disorders such as osteopetrosis, prolonged lead poisoning, Gaucher's disease, severe thalassaemia and cartilage dysplasias

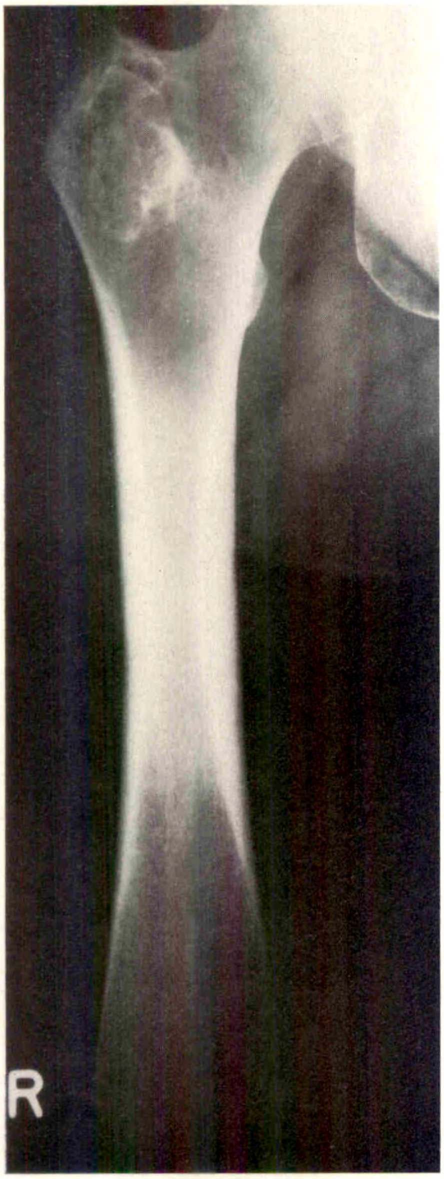
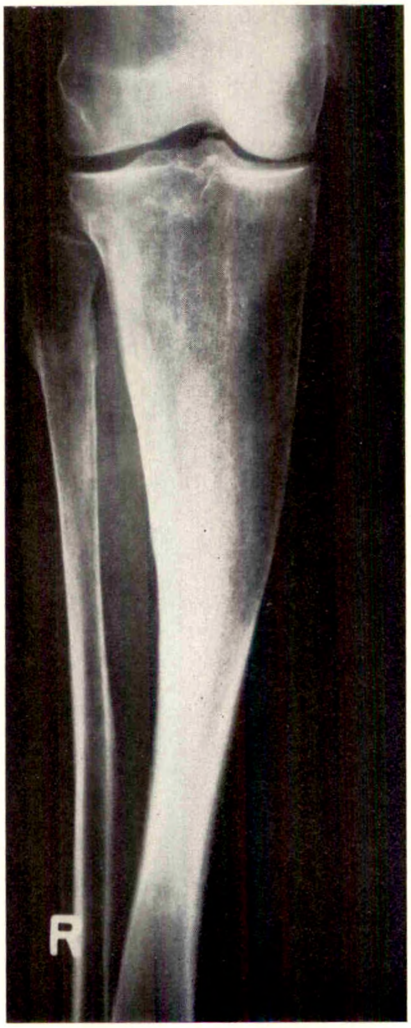


FIG. 10. *Case 1.*
The proximal extension of the "Erlenmeyer flask" deformity and endosteal cortical thickening are evident.



A *Patient 1.*
FIG. 11.

such as Ollier's disease and diaphyseal aclasis. However these conditions have distinctive clinical features and other characteristic radiological findings of their own.

ACKNOWLEDGMENTS

We are grateful to Mrs. S. Henderson for the illustrations and Miss B. Neumann for typing the manuscript.

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REFERENCES

BAKWIN, H. and KRIDA, A., 1937. Familial metaphyseal dysplasia. *American Journal of Diseases of Children*, *53*, 1521–1527.

FELD, H., SWITZER, R. A., DEXTER, M. W., and LANGER, E. W., 1954. Familial metaphyseal dysplasia. *Radiology*, *65*, 206–212.

GORLIN, R. J., SPRANGER, J., and KOSZALKA, M. F., 1969. Genetic craniotubular bone dysplasias and hyperostoses. A critical analysis. *Birth Defects—Original Article Series, Part V*, *4*, 79–95.

GORLIN, R. J., KOSZALKA, M. F., and SPRANGER, J., 1970. Pyle's disease (familial metaphyseal dysplasia). *Journal of Bone and Joint Surgery*, *52A*, 345–354.

HAMMAN, C. A., 1910. An abnormality in the form of the femur. *Cleveland Medical Journal*, *9*, 710.

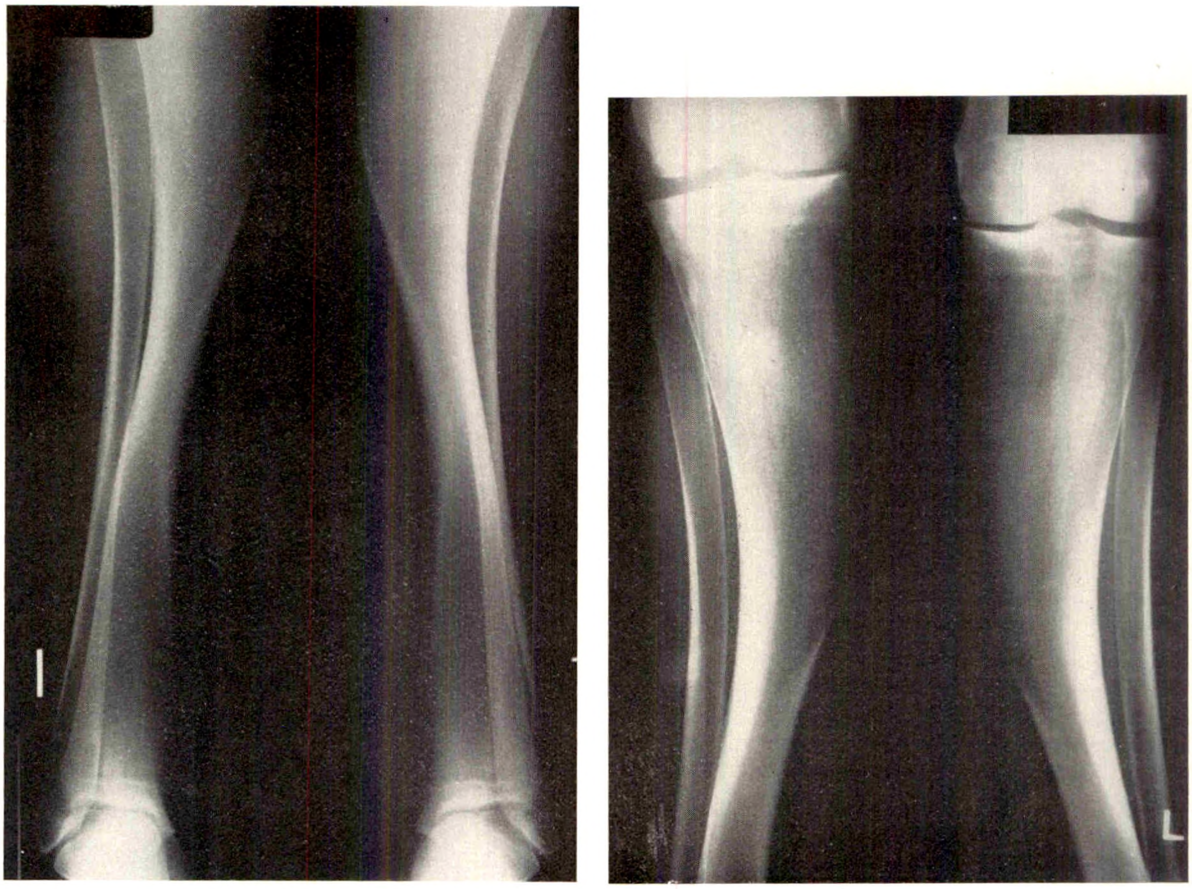
HERMEL, M. B., GERSHON-COHEN, J., and JONES, D. T., 1953. Familial metaphyseal dysplasia. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, *70*, 413–421.

HOLT, J. F., 1966. The evolution of cranial metaphyseal dysplasia. *Annales de Radiologie*, *9*, 209–214.

International Nomenclature of Constitutional Diseases of Bone, 1977. *American Journal of Roentgenology*, *131*, 352–354.

1978. *Annales de Radiologie*, *21*, 253–258.

JACKSON, W. P. U., ALBRIGHT, F., DREWRY, G., HANELIN, J., and RUBIN, M. I., 1954. Metaphyseal dysplasia,



B *Patient 2.*

C *Patient 3.*

FIG. 11.

The tibiae show predominantly proximal flaring, with lateral S-shaped bowing.

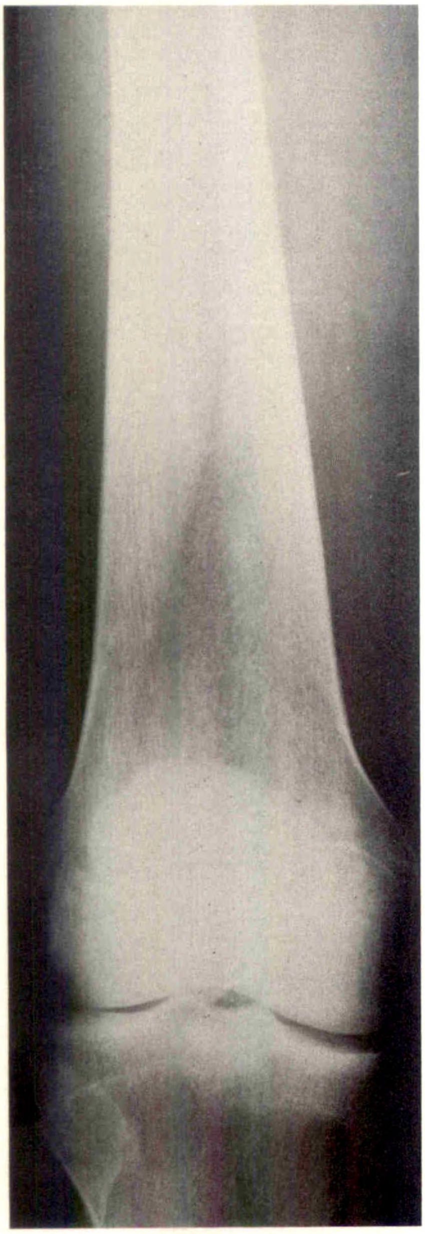


FIG. 12.

Mild undertubulation of distal femur in a heterozygote or clinically normal carrier of the gene in the family of patients 1 and 2.

epiphyseal dysplasia, diaphyseal dysplasia and related conditions. *Archives of Internal Medicine*, *96*, 871–887.

KOMINS, C., 1954. Familial metaphyseal dysplasia (Pyle's disease). *British Journal of Radiology*, *27*, 670–675.

MABILLE, J.-P., BENOIT, J.-P., and CASTERA, D., 1973. Dysplasie metaphysaire de Pyle. *Annals of Radiology*, *16*, 723–730.

MORI, P. A. and HOLT, J. F., 1956. Cranial manifestations of familial metaphyseal dysplasia. *Radiology*, *66*, 335–343.

PYLE, E., 1931. Case of unusual bone development. *Journal of Bone and Joint Surgery*, *13*, 874–876.

RAAD, M. and BEIGHTON, P., 1978. Autosomal recessive inheritance of metaphyseal dysplasia (Pyle disease). *Clinical Genetics*, *14*, 251–256.

ROSS, M. W. and ALTMAN, D. H., 1967. Familial metaphyseal dysplasia. *Clinical Pediatrics*, *6*, 143–149.

SPRANGER, J. W., LANGER, L. O., and WIEDEMANN, H. R., 1974. Bone dysplasias. *An atlas of Constititional Disorders of Skeletal Development* (Gustav Fisher Verlag, Stuttgart) pp. 316.

WALKER, N., 1966. Pyle's disease or cranio-metaphyseal dysplasia. *Annales de Radiologie*, *9*, 197–207.

1979, *British Journal of Radiology*, *52*, 441–443 JUNE 1979

Metaphyseal fractures in osteogenesis imperfecta

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The Children's Hospital, Birmingham

(Received November, 1978)

ABSTRACT

Forty-one children with osteogenesis imperfecta have been reviewed. A minority (7/41) showed small metaphyseal fractures, resembling those seen in non-accidental injury, but in all of these there was obvious generalized bone disease so that confusion with non-accidental injury did not occur.

In non-accidental injury of childhood (the "battered baby" syndrome), the possibility of fragile bones may be raised. Therefore the findings in 41 children seen at the Children's Hospital with osteogenesis imperfecta have been reviewed. Special attention has been paid to the occurrence of the type of metaphyseal fracture that is often seen in non-accidental injury, *i.e.* a small flake detached near the epiphyseal line.

The 41 children had received 316 radiological examinations, an indication of the large number of radiographs that was available for review.

FINDINGS

1. *Osteoporosis.* In addition to their fractures, all 41 children showed osteoporosis, easily detected in 37 but mild in four. These four all had multiple wormian bones in the skull and none had metaphyseal fractures.

2. *Wormian bones* were present in 33 out of 36 children where skull radiographs were available. The three children without wormian bones all showed easily recognized osteoporosis and none had metaphyseal fractures.

3. *Small metaphyseal fractures* were present in seven of the 41 children (Table I). In these seven there was an obvious generalized skeletal disease with easily recognized osteoporosis, abnormal bone modelling and major fractures in addition to the detached metaphyseal flakes (Fig. 1). In all seven there were wormian bones in the skull. In six of the seven (in one child there was no follow-up), further fractures were seen after the diagnosis of osteogenesis imperfecta had been made and none of these later fractures were of metaphyseal type.

COMMENT

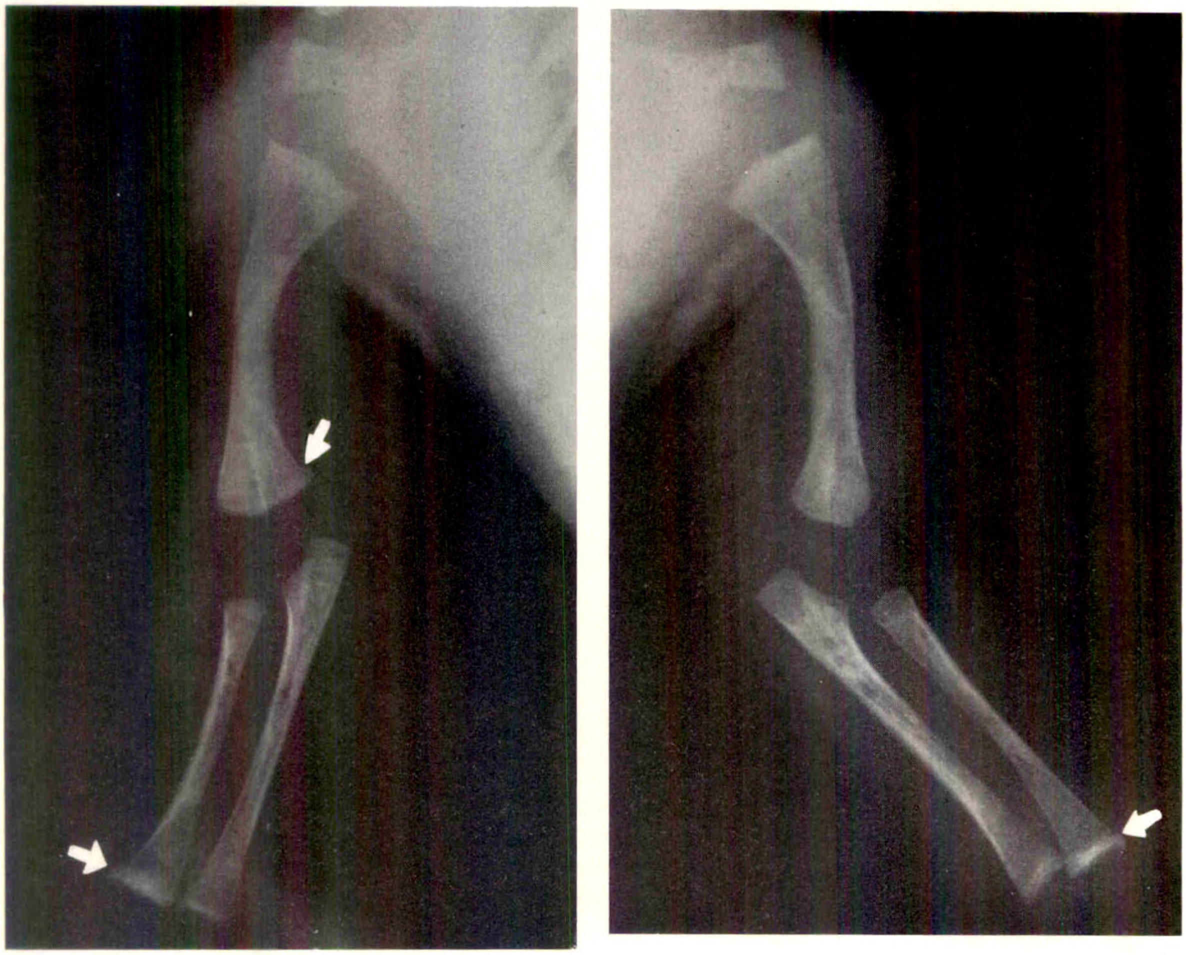
In 37 of the 41 children reviewed, there was no radiological difficulty whatsoever in making a diagnosis of osteogenesis imperfecta. Even in the remaining four there was osteoporosis, albeit less obvious, plus the presence of multiple wormian bones.

The presence of wormian bones is clearly a useful diagnostic sign. In the four children where they were not present, osteoporosis was not in doubt; conversely, where osteoporosis was slight,

TABLE I

Name	Age when MF seen	Sites of MF	General appearance of bones	Wormian bones
A.H.	1 day	Upper L. humerus	Porosis with gross abnormality	Present
R.W.	2 days	Lower R. humerus; Lower R. & L. radius	Porosis with gross abnormality	Present
B.M.	1 week	Upper L. humerus; Lower R. humerus; Lower R. & L. radius	Porosis with gross abnormality	Present
C.S.	1 month	Upper L. radius; Lower L. ulna	Porosis with gross abnormality	Present
S.B.	5 months	Lower L. tibia	Porosis with gross abnormality	Present
R.C.	14 months	Lower L. radius	Porosis with gross abnormality	Present
B.B.	3 years	Lower R. ulna	Porosis with gross abnormality	Present

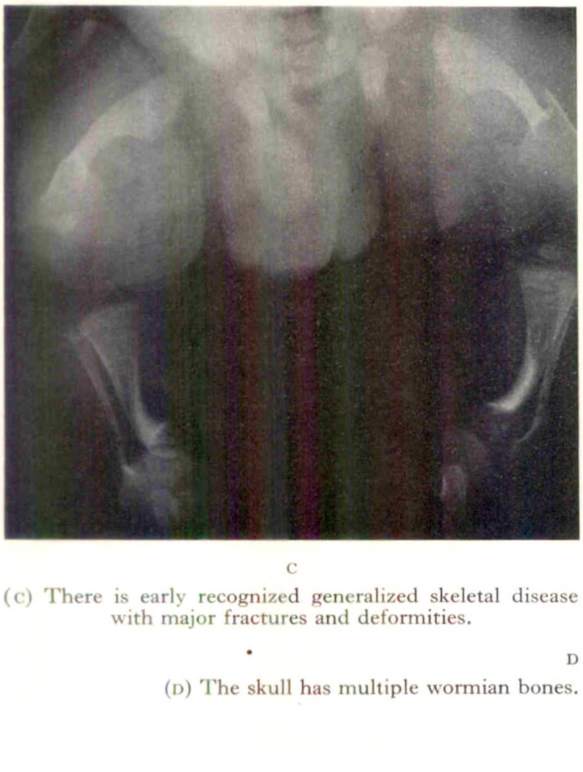
MF = metaphyseal fracture.



A FIG. 1. B

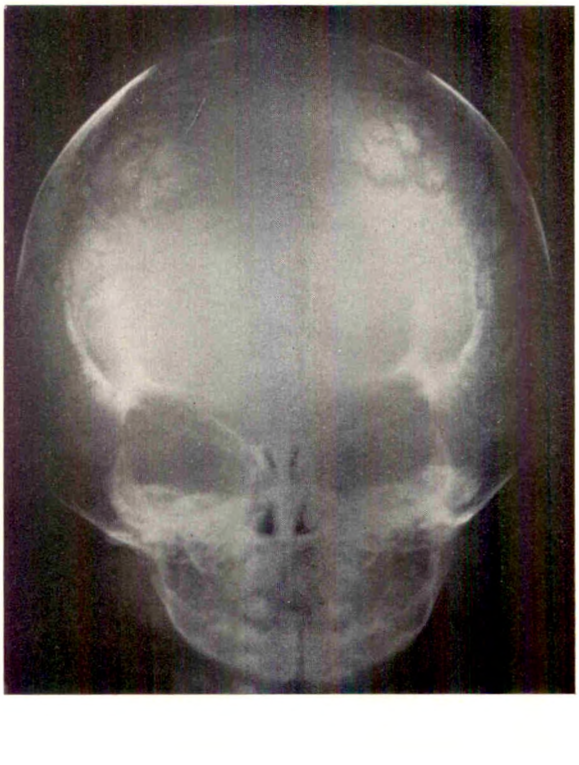
R.W., age 2 days.

(A and B) There are small metaphyseal fractures at the lower end of the right humerus and at the lower end of each radius.



C

(C) There is early recognized generalized skeletal disease with major fractures and deformities.



D

(D) The skull has multiple wormian bones.

wormian bones were present to reinforce the diagnosis.

A minority of children showed small metaphyseal fractures, resembling those seen in non-accidental injury. In all of these there was an obvious generalized disease of bone with easily recognized osteoporosis, abnormal bone modelling, deformities, major fractures and wormian bones, in addition to the detached metaphyseal flakes. Confusion with non-accidental injury did not occur.

Book reviews

Telescreen and Radiographic Examination of Urinary Transport. By Endre Hajós, pp. 117, illus., 1978. (Akadémiai Kiadó—Publishing House of the Hungarian Academy of Sciences—Budapest). $10.50.
ISBN 963–05–1507–5.

"Functional radiodiagnostics of the kidney is an oft-desired and highly desirable ideal which, however, is not easily achieved. This work has set the aim to get one step nearer to this ideal. . .

"In the last 15 years (the) image intensifier has been extensively used for the examination of the urinary tract. In the present study a great number of patients were examined and the motility changes were recorded over a relatively long period of time. This allowed us to make new observations and to draw some conclusions regarding the site and frequency of the renal pacemaker."

These are two paragraphs from the Preface of this well produced monograph. They give a fair indication of the range and style of the work. It is a painstaking, sober record of 800 IVUs, mostly adult, using fluoroscopy of the upper urinary tracts and only a few radiographs. The author presents evidence that this did not result in high radiation burdens in these patients.

What happens in normal as well as abnormal states is documented with care. Such studies of the patterns of contraction of the upper urinary tract already have a long history. Many radiologists will have learnt for themselves how fluoroscopy can often resolve points of diagnostic difficulty, particularly, in confirming or refuting a doubtful ureteric stone. However, there is real value in having so much first hand information on the human system assembled in one good small book. There is for instance the authoritative finding that contractions commonly begin in the renal pelvis at a site just above the pelviureteric junction—the human pacemaker is here, not in the calices (bifid systems excepted).

In work so much concerned with tone, contractility and movement, the absence of any pressure measurements is perhaps rather a drawback. This is particularly so in the final part of the book, dealing with "the orthostatic reaction". This is said to be a reflex contraction of the upper urinary tract on standing up. The author is aware of alternative explanations for the IVU findings in the erect posture (*e.g.* gravity), and argues his case skilfully. I found this the most interesting section of the book, nicely provocative even if the reader may dissent. Why *is* the ureter below a stone sometimes dilated and idle?

I think this is a stimulating contribution to the field of urodynamics. Perhaps not every X-ray department will wish to own a copy, but larger libraries and anyone interested in the subject should have a look at Hajós.

THOMAS SHERWOOD.

The Diagnostic Limitations of Computerised Axial Tomography. Edited by J. Bories, pp. xi + 220, 1978 (Springer Verlag, Berlin, Heidelberg, New York) DM54/$27/£14·50.
ISBN 3-540-08593-9

The profound changes that have occurred in the diagnostic management of patients with neurological problems since Hounsfield first presented computed tomography to the world have inevitably resulted in a vast literature, most of which extolled its "virtues" without perhaps enough emphasis placed on its "vices". It is therefore welcome to find at last a scientific meeting whose main purpose has been to criticize CT, to define its limitations and perhaps to "get it in perspective".

The book edited by Dr. Bories, derives from papers presented at the 6th Congress of the European Society of Neuroradiology in Dijon in September, 1976. The papers from many major world centres cover a wide variety of pathology and most accurately demonstrate the limitations of computed tomography as well as giving numerous useful, practical hints. It is divided into five parts—cerebral tumours; orbit and skull base; infarcts, oedema and sub-dural haematomas; CT and other techniques; CT accuracy and future aspects. There are however, few papers that compare the accuracy of CT with other neuroradiological procedures, indeed in some areas the pendulum has already begun to swing back to more conventional examinations. In this context I was most interested to see, as I have always thought, how little extra help is forthcoming as a result of "gazing at print-outs".

It is over two years since the meeting was held and most of the newer developments referred to by Professor Taveras have already been reached. Scan times of one to two seconds, gating for the heart and reconstruction of picture slices, both coronally and sagitally, as well as higher resolution scans for the spinal canal are now available on a number of machines. Indeed further technical advances are expected each year. Nevertheless the problem areas (skull base, perichiasmatic region, posterior fossa etc.) still remain essentially unchanged, as does sometimes the overlap in appearances between those cases which require surgery and those in which surgery is unwise if not dangerous. It is apparent that there is no substitute for an experienced radiologist in reducing the false positive and negative rates. Such experience takes time to acquire, but with the aid of this book many of the problem areas have not only been highlighted, but elucidated. The book assumes a reasonable knowledge of the subject, but is undoubtedly essential reading to anyone who wishes to become competent in this subject.

D. P. E. KINGSLEY.

1979, *British Journal of Radiology*, *52*, 444–451

A review of the radiological anatomy of the round window

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ABSTRACT

Experimental studies on dried temporal bones in various projections combined with studies of the anatomical details marked with metal wires and/or barium paste have been performed to define the round window and its anatomical relation to surrounding structures.

The exact plane of the round window was not found to be tomographically demonstrable and the term to describe the dehiscence in the lateral wall of the promontory below and posterior to that of the oval window should be the niche of the round window. Previous radiologically described pathological changes at the round window should be reviewed.

Since the late 1950's thorough investigation of the temporal bone with multidirectional tomography has taken place. Many articles and books on the radiological anatomy of the temporal bone, its normal variations and pathological changes have been published. Areas in reach of the surgeon such as the internal acoustic meatus, the oval (vestibular) window and the endolymphatic duct achieved complete and skilful studies which established the radiological anatomy of these areas.

Less interest, however, has been given to the region of the round window, being of minimal surgical interest.

In the antero-posterior (AP) and semi-axial projections the round window has been described as a dehiscence in the lateral wall of the promontory below that of the oval window. There has been some difference in the description of the level of the window in earlier articles. François and Barrois (1959) demonstrated the dehiscence of the round window 2 mm posteriorly to that of the oval window. Mündnich and Frey (1959) described the dehiscence being at the same level or slightly ventral to that of the oval window. Valvassori (1963) described its location 3 mm posterior to that of the oval window. All these measurements were done in the AP projection. In the semi-axial projection, Gros *et al.* (1962) illustrated the round window located 4 mm posterior to that of the oval window. Many authors have stated that the dehiscence is not always clearly visualized, and that it is best seen in the Stenvers and the lateral projections.

The size of the round window has been measured as 2 mm in diameter by Gros *et al.* (1962), and by Rovsing (1970) as 1–2 mm in height (in 70% of his cases), 2–3 mm in length (in 60% of his cases).

Few authors have described a niche of the round window (Valvassori 1965; Quinto and Himadi 1974; Valvassori and Buckingham 1975; Schaefer 1976). Of these Valvassori uses the term more frequently and clearly. But even these authors use the term round window in their text and illustrations. Only few authors have described pathological changes in the round window area, defined as "a dehiscence in the lateral wall of the promontory below and posterior to that of the oval window", in otosclerosis (Mündnich 1961; Frey *et al.* 1967; Rovsing 1970; 1974); and in congenital deformities, (Phelps *et al.* 1977).

The aim of this work is to review the radiological anatomy of the round window and to discuss the appearance of this structure on tomograms.

ANATOMY

The fossula or niche of the round (cochlear) window is an irregularly prismatic recess with rounded angles, which extends from a point near the bottom of the middle ear upwards, inwards and forwards beneath the arch of the first turn of the cochlea. One surface of the niche is directed downward and represents the tympanic aditus of the fossula. Much of the rim of this opening is formed by the overhanging ledge of the promontory, produced by the arch of the first coil of the cochlea.

The cochlear fenestra lies in the antero-superior wall of the fossula. Its bony margin is formed posteriorly by part of the cochlear capsule, anteriorly by part of the inner portion of the bony promontory and superiorly by the two bony spiral laminae. The window is rounded in shape, and its plane is vertical. The cochlea is separated from the fossula by the

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Reprint requests to H. Rovsing.

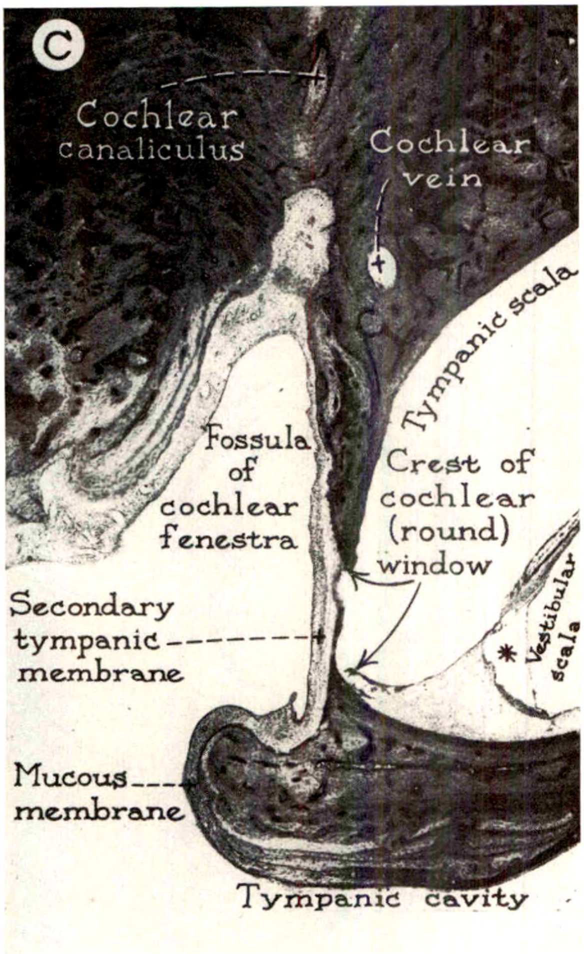


FIG. 1.

A transverse section of a temporal bone showing the anatomy of the region of the round window. (From Anson and Donaldson, 1967.)

secondary tympanic membrane, or round window membrane, which is completely out of view from the tympanic cavity, and may be brought into view only by removing the overhanging bone of the promontory (Bast and Anson, 1952).

The secondary tympanic membrane is a thin plate of connective tissue, whose lateral surface is covered by the mucosal lining of the middle ear. The membrane is attached to the crista fenestrae cochleae (Anson and Donaldson, 1967) (Fig.1).

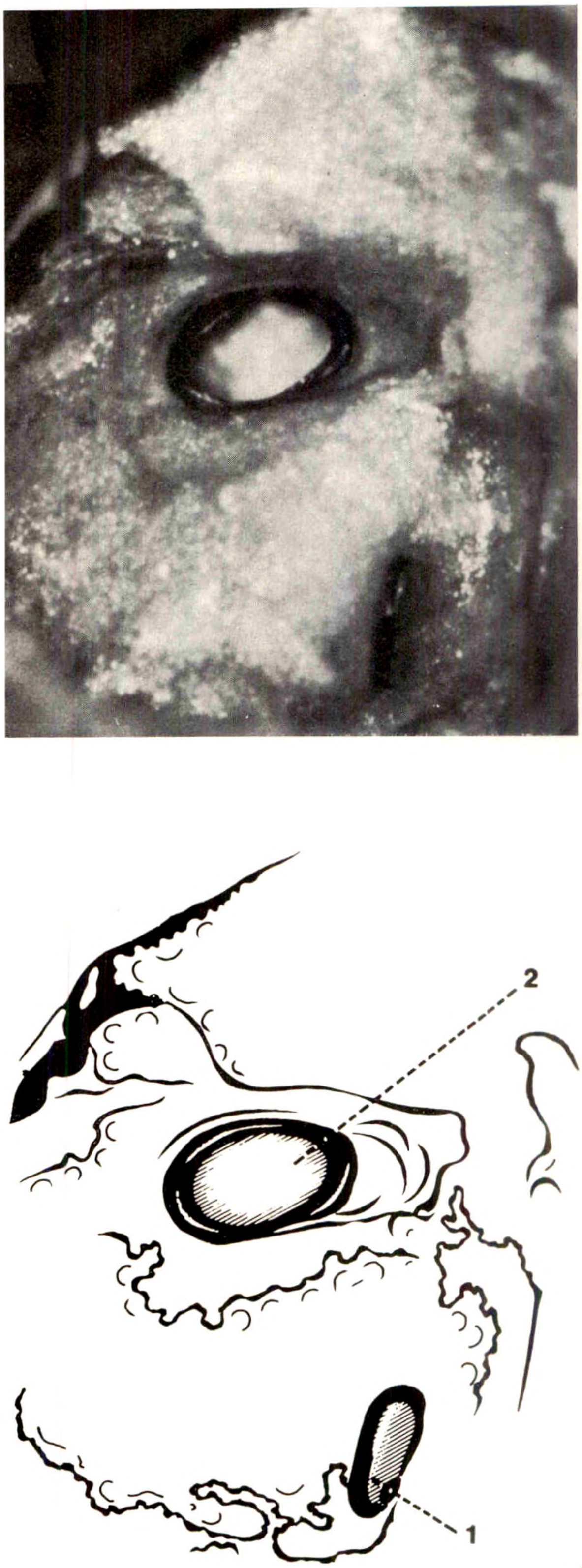


FIG. 2.

Oto-microscopic photograph of a dried left temporal bone specimen with metallic wires fixed at the external opening of the niche to the round window (1) and at the oval window (2).
1. The tympanic opening of the niche of the round window.
2. The oval window.

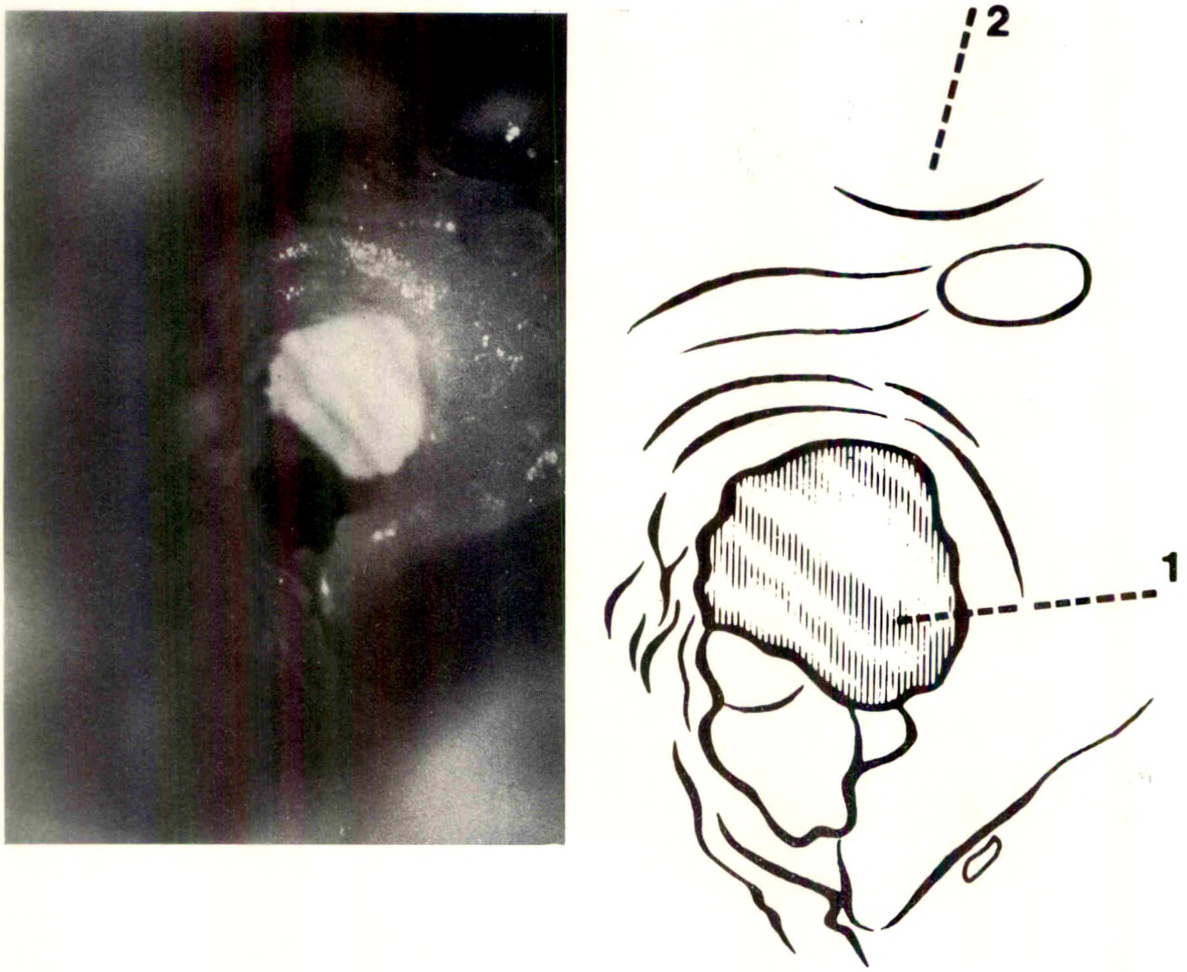


FIG. 3.

Oto-microscopic photograph of a right anatomical temporal bone specimen after complete filling of the niche of the round window. Barium paste is seen at the tympanic opening of the niche (1). The oval window is seen upwards and forwards (2).

In a horizontal section of an adult specimen Wolff *et al.* (1957), described a niche 4 mm deep to the surface of the promontory. The round window was measured to have an area of 2 mm^2. Its framed membrane has a larger area which is difficult to calculate, since it does not lie in a single plane.

Less than 2 mm behind the posterior margin of the round window, the anterior surface of the ampullary end of the posterior semicircular canal is situated (Valvassori and Buckingham, 1975).

MATERIAL AND METHOD

The material consisted of two dried temporal bones (without soft tissues) and 11 anatomical temporal bone specimens with intact round window membranes. In order to visualize the anatomical landmarks by tomography, the specimens were prepared and examined in the following way:

1. The dried specimens were examined before and after fixing metallic wires shaped to fit the external (tympanic) opening of the niche of the round window, and the oval window (Fig. 2).

2. The anatomical temporal bone specimens were subdivided into the following groups:

(a) complete filling of the niche of the round window with barium paste (Fig. 3). Mucosal folds partially filling the niche had been removed before applying the barium;

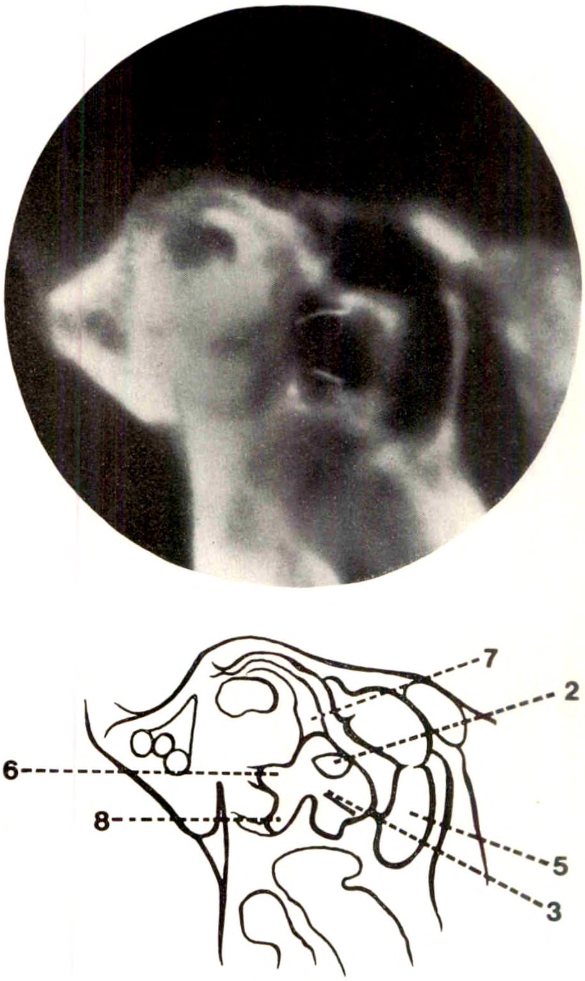


FIG. 5.

A lateral tomogram of an anatomical specimen with metallic wires fixed at the planes of the round (3) and the oval (2) windows. The round window is lacking distinct tomographically demonstrable landmarks.

2. The oval window
3. The plane of the round window
5. The tympanic cavity
6. The lateral semicircular canal
7. The superior semicircular canal
8. The posterior semicircular canal

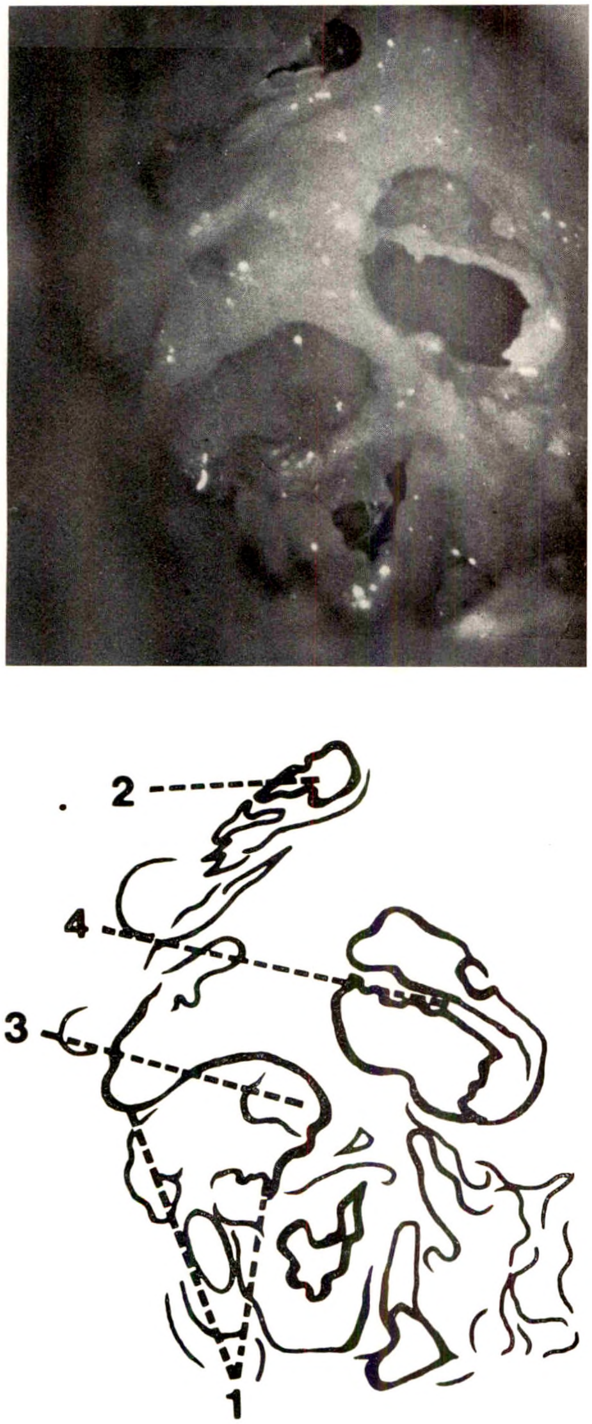


FIG. 4.

Oto-microscopic photograph of a right temporal bone after removing the promontorial bony covering of the niche and the beginning of the basal turn of the cochlea. The depth of the niche is the distance between its tympanic opening (1) and the round window membrane (3). The osseous spiral lamina at the basal turn of the cochlea is exposed (4). The oval window (2) is also seen.

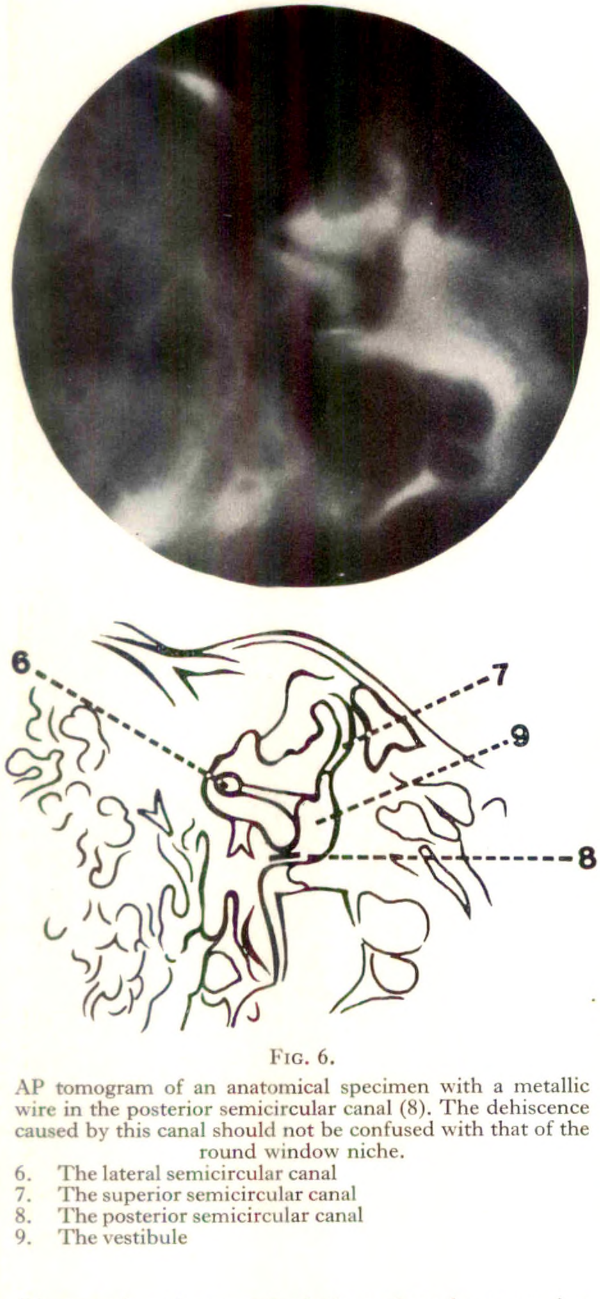


FIG. 6.

AP tomogram of an anatomical specimen with a metallic wire in the posterior semicircular canal (8). The dehiscence caused by this canal should not be confused with that of the round window niche.

6. The lateral semicircular canal
7. The superior semicircular canal
8. The posterior semicircular canal
9. The vestibule

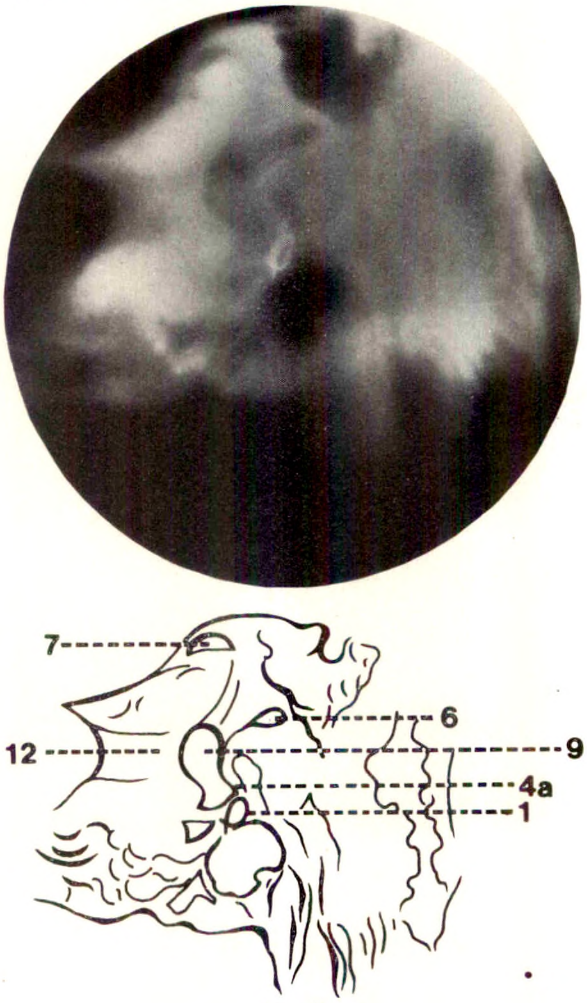


FIG. 7.

AP tomogram of a dried temporal bone showing a metallic wire at the opening of the niche of the round window (1). The term "round window niche" should be used to describe the dehiscence and not the term "round window".

1. The tympanic opening of the niche of the round window
4a. The promontory
6. The lateral semicircular canal
7. The superior semicircular canal
9. The vestibule
12. The internal auditory canal

(b) exposing the round window plane by removing the promontorial bony covering of the niche and the beginning of the basal turn of the cochlea (Fig. 4) and smearing the round window membrane with barium. In one of these specimens metallic wires were fixed at the oval and round windows (Fig. 5);

(c) inserting a metallic wire in the ampullary end of the posterior semicircular canal, reaching the vestibule (Fig. 6).

The specimens were examined with the Polytome U3 (Philips-Massiot), using the hypocycloid movement, in the AP, lateral, semi-axial, axial-pyramidal, Stenvers and submento-vertical projections.

FINDINGS

In Fig. 7 an AP projection of a dried temporal bone with inserted metallic wire is shown. The wire delineates the opening of the niche (fossula) of the round window towards the middle ear cavity. This lateral opening of the niche corresponds to the structure so consistently described previously as "the round window".

The temporal bone examined in the semi-axial projection (Fig. 8) demonstrates the lateral (tympanic) opening of the round window niche. The promontory is projected lateral to this opening and may cause a misinterpretation of the round window niche as being obliterated.

Tomograms in the AP, semi-axial and Stenvers' projections of the specimen with complete filling of the round window niche with barium paste demonstrate the depth of the window niche in the different projections (Fig. 9A, B, C). The antero-superior aspect of the niche, where the round window is situated, is not an exactly localizable or measurable distance.

With metallic wires inserted into the plane of both the oval and the round window, the tomogram in the lateral projection (Fig. 5) reveals the windows situated almost on a perpendicular line, the oval window facing laterally, the round window facing postero-inferiorly. As in other projections, the bony margins of the round window membrane are indistinct. Specimens with barium-paste smeared round window membrane fortify the impression of indistinct, not tomographically visible, bony margins of the round window.

Figure 6 is a semi-axial tomogram of a specimen with a metallic wire inserted in the ampullary end of the posterior semicircular canal. The dehiscence in the infero-lateral aspect of the vestibule, seen in this specimen 3 mm posterior to that of the niche to the round window, should not be mistaken for a round window niche, particularly if the niche was not clearly visualized. This may explain the early description of a round window 3–4 mm posterior to that of the oval window, in the AP and semi-axial projections, possibly describing the ampullary end of the posterior semicircular canal. In our specimens, the dehiscence of the round window niche was seen in a range of 2 mm posterior to, and up to the same level of the oval window.

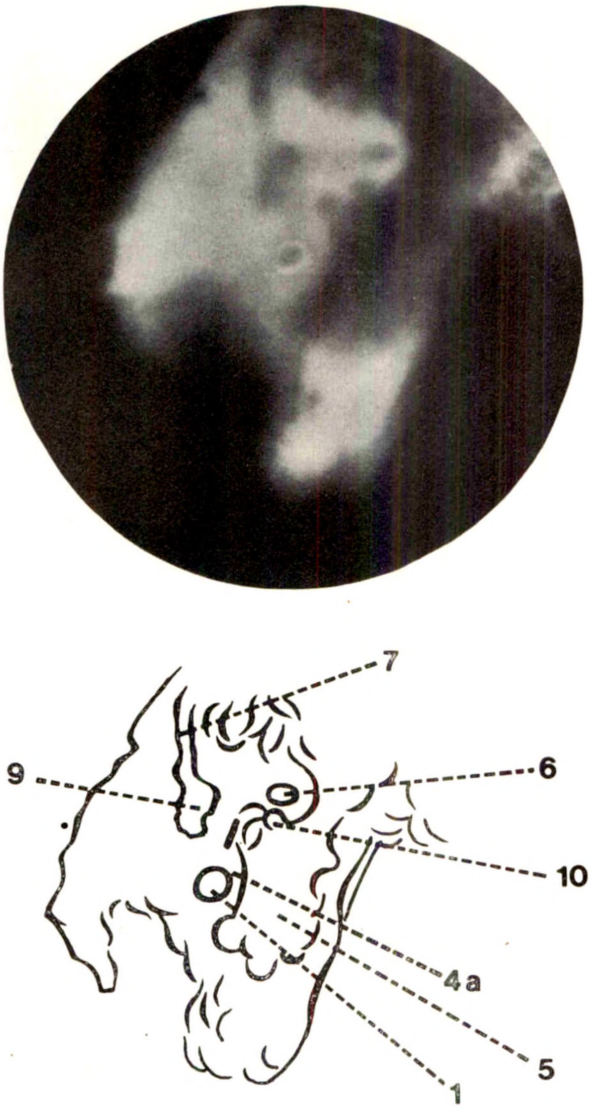


FIG. 8.

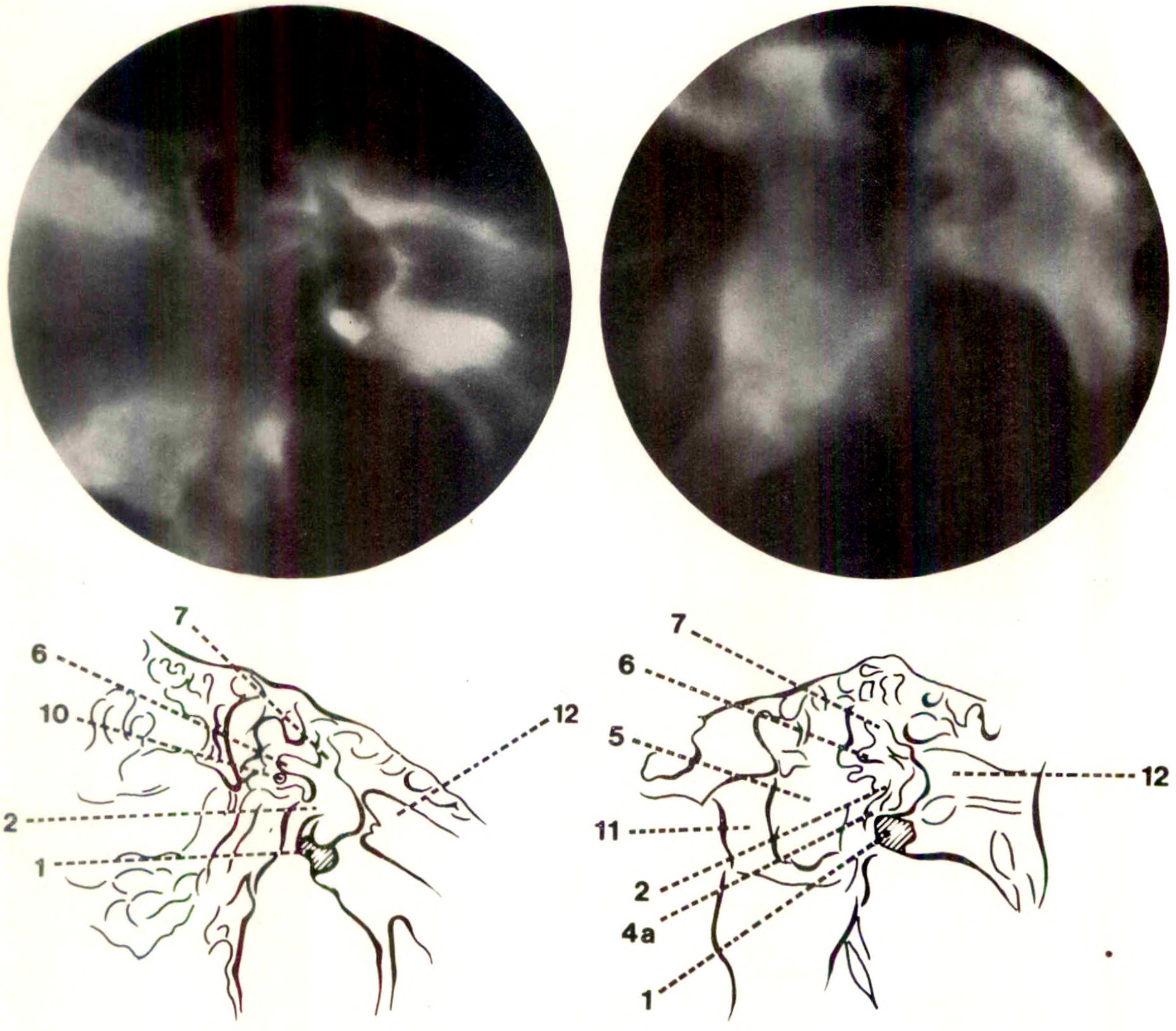
A semi-axial tomogram of a dried temporal bone specimen with a metallic wire fixed at the lateral opening of the niche of the round window (1). The opening of the niche of the round window (1) is projected medial to the promontory (4a). This should not be mistaken for an obliterated round window niche.

1. The tympanic opening of the niche of the round window
4a. The promontory
5. The tympanic cavity
6. The lateral semicircular canal
7. The superior semicircular canal
9. The vestibule
10. The canal of the facial nerve

CONCLUSIONS

The term "niche of the round window" should be used instead of the "round window" when describing this dehiscence in the promontory. Our examinations indicate that the plane of the round window lacks distinct tomographically demonstrable anatomical landmarks.

Non-visualization of the niche of the round window in one projection does not necessarily mean an



A

B

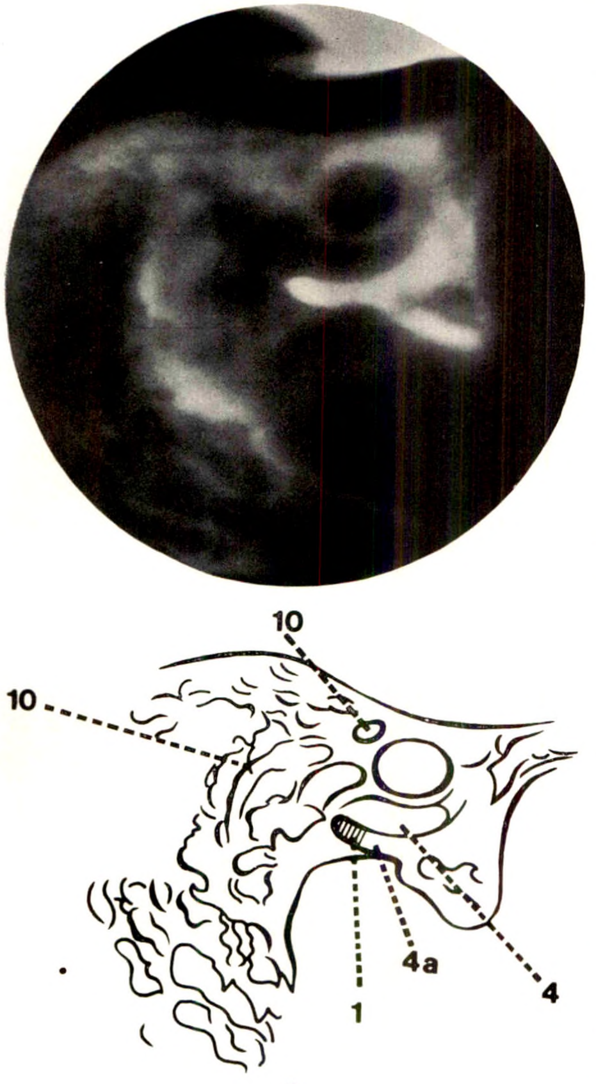
FIG. 9.

AP (A), semi-axial (B) and Stenvers (C) tomograms of an anatomical temporal bone with complete filling of the niche of the round window with barium paste. The exact localization of the plane of the round window is not tomographically possible.

1. The tympanic opening of the niche of the round window
2. The oval window
4. The basal turn of the cochlea
4a. The promontory
5. The tympanic cavity
6. The lateral semicircular canal
7. The superior semicircular canal
10. The canal of the facial nerve
11. The external auditory canal
12. The internal auditory canal

obliterated or absent niche. The dehiscence of the ampullary end of the posterior semicircular canal should not be mistaken for the dehiscence of the round window niche, particularly if the latter is not clearly visualized.

Lastly, earlier statements, measurements and



C

FIG. 9.

evaluation of possible pathological changes of the round window, previously radiologically described, should be reviewed.

REFERENCES

ANSON, B. J., and DONALDSON, J. A., 1967. *The Surgical Anatomy of the Temporal Bone and Ear.* (W. B. Saunders Company, Philadelphia—London).

BAST, T. A., and ANSON, B. J., 1952. The development of the cochlear fenestra, fossula and secondary tympanic membrane. *Quarterly Bulletin of North-western University Medical School, 26,* 344.

FRANÇOIS, J., and BARROIS, J., 1959. Anatomie tomographique de l'os temporal normal. *Annales de Radiologie, 2,* 71–98.

FREY, K. W., KLEMM, J., and MICHEL, M., 1967. Tomographie der Otosklerose. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuclearmedizin, 106,* 428–440.

GROS, CH., WALTER, J. P., BLOCH, J., and BOURJAT, P., 1962. La paroi labyrinthique: aspects tomographiques. *Journal de Radiologie d'Electrologie et de Médecine Nucléaire, 43,* 253–258.

MÜNDNICH, K., and FREY, K. W., 1959. *Das Röntgenschichtbild des Ohres,* 1. ed. (Thieme, Stuttgart).

MÜNDNICH, K., 1961. Die Radiologie der Otosklerose. *Fortschritte der Hals-Nasen-Ohrenheilkunde, 8,* 328–347.

PHELPS, P. D., LLOYD, G. A. S., and SHELDON, P. W. E., 1977. Congenital deformities of the middle and external ear. *British Journal of Radiology, 50,* 714–718.

QUINTO, F. C., and HIMADI, G. M., 1974. Tomographic anatomy of the ear. *Radiological Clinics of North America, 12,* 405–417.

ROVSING, H., 1970. Otosclerosis. A tomographic-clinical study. *Acta Radiologica (Stockholm) Supplementum 296.*

ROVSING, H., 1974. Fenestral and cochlear otosclerosis. *Radiological Clinics of North America, 12,* 505–515.

SCHAEFER, R. E., 1976. Roentgen anatomy of the temporal bone. In: LITTLETON, J. T., *Tomography, Physical Principles and Clinical Applications. Golden Diagnostic Radiology,* pp. 244–248 (Williams & Wilkins Company, Baltimore).

VALVASSORI, G. E., 1963. Laminagraphy of the ear. *American Journal of Roentgenology, 89,* 1155–1178.

1965. Otosclerosis: a new challenge to roentgenology. *American Journal of Roentgenology, 94,* 566–575.

VALVASSORI, G. E., and BUCKINGHAM, R. A., 1975. *Tomography and Cross Sections of the Ear* (Thieme, Stuttgart).

WOLFF, D., BELLUCCI, R. J., and EGGSTON, A. A., 1957. *Microscopic Anatomy of the Temporal Bone* (Williams & Wilkins Company, Baltimore).

Book review

Medical Terminology in Hospital Practice. By P. M. Davies, pp. 375, 1978 (William Heinemann, London), £4·95.
ISBN 0–433–07183–4

This useful reference book is summed up adequately in its sub-title "a guide for all those engaged in professions allied to medicine". It is neither text book nor dictionary but gives useful descriptions and explanations of terms related to medicine and is an aid to anyone having to use medical terminology. This volume, now in its third edition, can be strongly recommended for reference to students and radiographers or anyone finding it necessary to use medical terminology in the performance of their duties.

In particular emphasis is laid, where appropriate, on terminology relative to radiology and the practice of radiography.

This reference book is a valuable asset to members of the staff and should be readily available to all those needing to refer to medical terminology about which they are unsure.

L. SURRY.

1979, *British Journal of Radiology*, *52*, 452–457

Intravenous cholangiography in childhood

By J. B. Witcombe, F.R.C.R., D.C.H.,† R. Horwitz, M.B., Ch.B.* and B. J. Cremin, F.R.C.R., F.R.A.C.R.‡

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(*Received July, 1978 and in revised form November, 1978*)

Abstract

Intravenous cholangiography (IVC) was performed on 102 children aged between one and 13 years. Eighty of the patients who were non-icteric were divided into four groups and received contrast medium containing either 53, 75, 106 or 150 mg iodine/kg body weight by intravenous injection over ten minutes.

Complete demonstration of the common bile duct (CBD) was achieved in 85% of patients and in a similar proportion of all age groups. There was some delay in opacification of the CBD in young children but this was not of practical significance. The two higher dosage regimen gave significantly better results than the two lower dosages ($p < 0.001$) and this improvement was evident in the young and older age groups.

Nausea and vomiting occurred as side effects in 6%. In eight patients in whom there was inadequate demonstration by the standard IVC, an infusion technique over 3–8 hours was carried out. This improved the demonstration in three children with diagnostic results in two.

Intravenous cholangiography (IVC) is an uncommon investigation in childhood and techniques are based on adult experience.

The demonstration of bile ducts is inconsistent in infants (Reichelderfer and van Hartesveldt, 1955; Nahum *et al.*, 1969), but Fahr *et al.* (1977) reported good results in 23 children aged between three and 15 years. However, the success rate in children at different ages and optimum exposure times have not been reported. Gordon and Ross (1977) stated that excretion may be more rapid in children, Nahum *et al.* (1969) that the biliary tree may only be seen on late films, while Fahr *et al.* (1977) found that the best exposure times were similar to those in adults. The most satisfactory dosage of contrast medium for children of different sizes has not been critically assessed in clinical practice and although the incidence of side-effects is thought to be low in children (Chaumont *et al.*, 1974; Fahr *et al.*, 1977), only small paediatric series have previously been reported.

This lack of information led us to study a series of children in Cape Town where IVC is frequently undertaken to demonstrate roundworms in the biliary tree (Cremin and Fisher, 1976). The patients presenting in this way provided a homogenous group for a clinical trial although the indication for IVC was unusual by western standards.

Material and Methods

In 1977 102 IVCs were carried out on children aged between one and 13 years. Most patients presented with acute abdominal pain and often with a history of having vomited or evacuated roundworms. The majority had been referred to us directly from the Out-patient Department, others had been treated as In-patients, with intravenous fluids, nasogastric suction or antispasmodics such as 'Buscopan' (hyoscine-N-butylbromide), while a few presented for radiological follow-up examination after treatment for biliary roundworms.

The patients were allocated to a dosage regime containing one of the following:

- I 53 mg/iodine per kg body weight (0.3 ml/kg Biligram injection (meglumine ioglycamate)).
- II 75 mg/iodine per kg body weight (0.3 ml/kg Biligrafin forte (meglumine iodipamide)).
- III 106 mg/iodine per kg body weight (0.6 ml/kg Biligram injection (meglumine ioglycamate)).
- IV 150 mg/iodine per kg body weight (0.6 ml/kg Biligrafin forte (meglumine iodipamide)).

Allocation was on a rotational basis except for some adjustment to ensure that all age groups were similarly represented in each dosage regime.

The first 20 patients in each of the four dosage regimens who fulfilled the following criteria were used for comparing the different dosages of contrast media. These 80 patients were all non-icteric, had no history of previous hepato-biliary surgery or liver disease and presented with either a provisional diagnosis of roundworms in the biliary system or for follow-up examination after medical treatment for biliary ascariasis.

Thirty-three were male and 47 female and the age distribution in each age group is illustrated in Fig. 1.

A control radiograph was exposed with the patient in a 15 deg "prone-oblique" position. The calculated amount of contrast medium was made up to 20 ml

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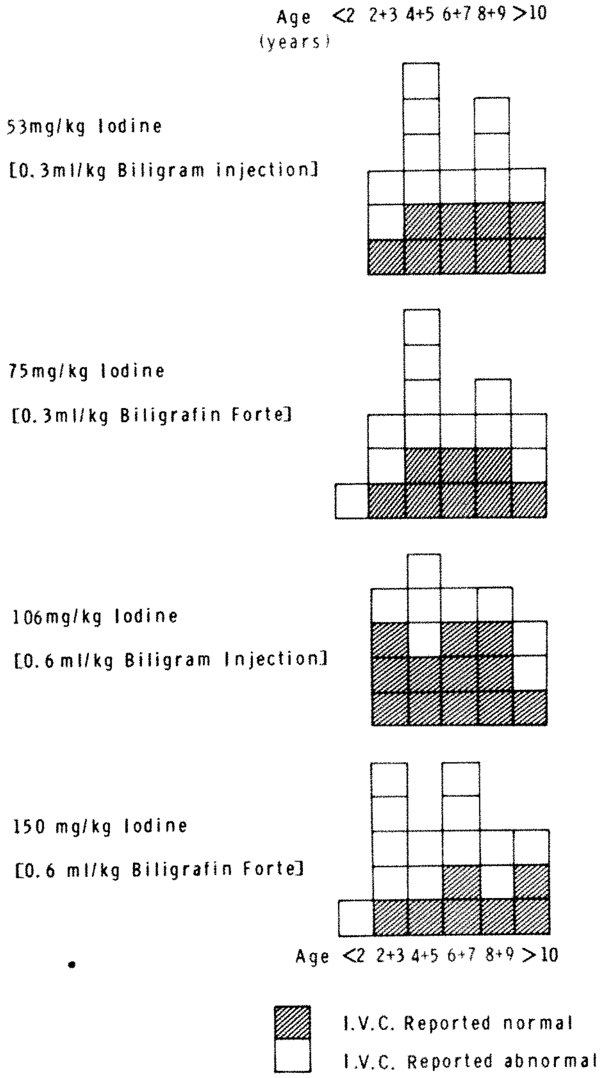

FIG. 1.

To show the age distribution of 20 patients in each of four dosage regimens, and the proportion of normal and abnormal examinations.

volume with normal saline and after a blood sample had been taken for liver function tests, the contrast medium was injected manually over a period of ten minutes. Plain radiographs were taken 20, 30, 45, 60 and 90 minutes after the start of the injection. When necessary, tomographs were taken after 45 minutes with the patient still in the 15 deg prone position. Delayed radiographs were exposed when indicated. Any side effects of the procedure were noted.

Eight patients whose standard IVC was not diagnostic proceeded to prolonged infusion cholangiography within 24 hours of the original examination. The same dose of contrast medium was used, diluted in 150 ml of normal saline and infused over 3–8 hours (Table I).

EVALUATION

All the radiographs were evaluated by two of the authors (JBW and RH) without knowledge of the dosage of contrast medium which had been given.

The examinations were ranked in order of the quality of CBD demonstration and the ranks of the examinations in each group compared using the Wilcoxon rank test. This test was also applied independently to the young patients (< 6 years) and older patients (> 6 years) to determine if the same dosage per kilogram gave the best results in both age groups. In addition, the demonstration of the CBD and gall bladder on each radiograph was graded on the following scales:

Common bile duct demonstration

Grade 0—No bile duct opacification.

Grade 1—Incomplete demonstration of the bile ducts.

Grade 2—Complete demonstration of the CBD.

Grade 3—Excellent demonstration of the CBD.

Gall-bladder demonstration

Grade 0—No gall-bladder opacification.

Grade 1—Poor or incomplete gall-bladder opacification.

Grade 2—Good gall-bladder opacification (judged adequate to demonstrate gall-stones).

Grade 3—Excellent gall-bladder opacification.

RESULTS

The CBD was demonstrated fully (Grade 2 or Grade 3) in 68 of 80 patients (85 %) and opacification was adequate to demonstrate roundworms in a further six cases (7.5 %). There was no significant difference in the proportion of ducts visualized at different ages (Fig. 2). Eighty-eight per cent of the ducts were seen in the 1–4 age group (15 out of 17) and 84 % in the 4–13 year olds (53 out of 63). The gall-bladder was opacified in 54 out of the 80 cases (67.5 %) by the 90-minute exposure but only well opacified (Grade 2 or Grade 3) in 34 cases (42.5 %).

DOSAGE

The two dosage regimes containing 106 mg iodine/kg or more gave significantly better demonstration of the common bile duct, and this improvement applied to the young ($p < 0.001$) as well as the older half of the series ($p < 0.001$).

TABLE I

Details of eight cases investigated by prolonged infusion cholangiography

Case number	Age	Liver function tests*	Contrast medium	Infusion duration (hr)	Result
7	11	N	0.3 ml/kg Billigram	5½	Improved from Grade 0 to Grade 3
13	3	N	0.6 ml/kg Biligram	9½	Improved to Grade 1
23	4	B –0.5 SGPT–458 AP –169	0.6 ml/kg Biligram	5½	No improvement
30	5	B –<0.5 SGPT–16 AP –202	0.6 ml/kg Biligram	3	No improvement
41	4	B –0.6 SGPT–210 AP –158	0.3 ml/kg Biligrafin forte	4½	No improvement
47	3	B –3.9 SGPT–21 AP –655	0.6 ml/kg Biligram	4	No improvement
48	10	N	0.6 ml/kg Biligram	4	No improvement
57	8	N	0.3 ml/kg Biligrafin forte	4½	Improved from Grade 1 to Grade 3

*Normal ranges: B. (bilirubin) <0.8 mg% S.G.P.T. – <30 i.u.
AP. (alkaline phosphatase) – <140 i.u. N is Normal

TABLE II

To show the number of cases achieving each grade for CBD and gallbladder opacification

Dosage regimen	No. of cases	No. of cases achieving each CBD grade				No. of cases achieving each gallbladder grade			
		0	1	2	3	0	1	2	3
52 mg/kg iodine as Biligram injection (0.3 ml/kg)	20	–	6	8	6	5	7	3	5
75 mg/kg iodine as Biligrafin forte (0.3 ml/kg)	20	–	4	9	7	8	7	–	5
106 mg/kg iodine as Biligram injection (0.6 ml/kg)	20	2	–	7	11	5	1	9	5
150 mg/kg iodine as Biligrafin forte (0.6 ml/kg)	20	–	–	8	12	8	5	2	5

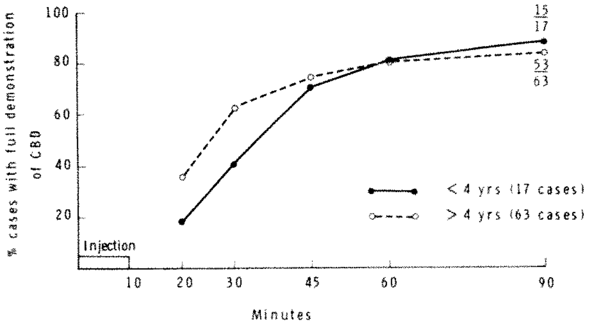

FIG. 2.

To illustrate the percentage of cases with full demonstration (Grade 2) of the CBD at each exposure time.

Table II shows that not only was the quality of the CBD demonstration better in the higher dosage regimes, but the proportion of diagnostic results (Grade 2 and Grade 3) was higher.

Despite the lower total iodine content, opacification of the gall-bladder was better in the two regimens using Biligram (ioglycamate) rather than Biligrafin forte (iodipamide) but the difference was not significant. Gall-bladder visualization was best with 0.6 ml/kg Biligram containing 106 mg iodine/kg.

EXPOSURE TIMING

Sixty-eight patients in whom the CBD was fully demonstrated (Grade 2 or Grade 3) were studied. Figure 2 illustrates the percentage of bile ducts demonstrated at each exposure time in these patients. There was delay in the opacification of the CBD in patients aged 1–4 years but by 45 minutes a similar proportion of ducts had been demonstrated in all age groups and maximum information about the CBD had been obtained in 87% cases. In no case did radiographs exposed after 90 minutes result in improved demonstration of the CBD. Occasionally the gall-bladder was better shown on delayed radiographs but only when it contained visible contrast medium at 90 minutes. The proportion of bile ducts demonstrated at each exposure time was similar in each dosage regime and was unaffected by the normality or abnormality of the studies.

SIDE EFFECTS

Six patients (6%) in the full series of 102 developed side effects shortly after contrast medium injection. One suffered from nausea and excessive salivation, and five vomited. Side effects followed regime IV in four patients, regime III in one and regime I in another.

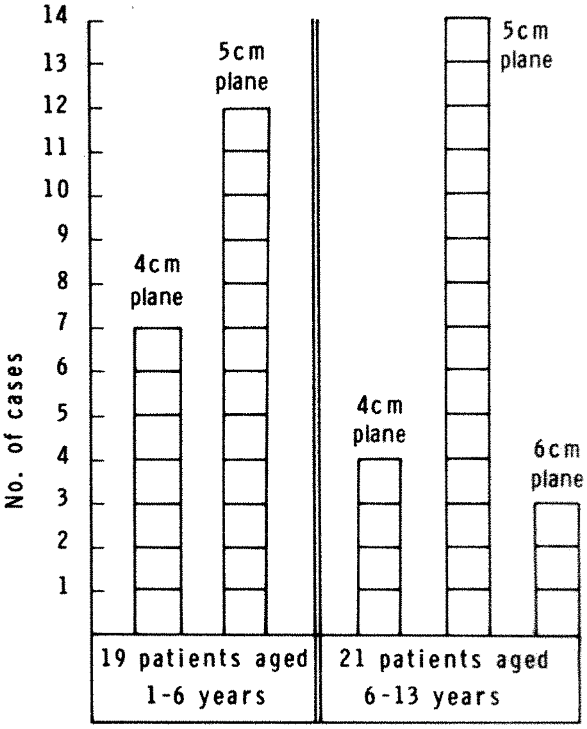

FIG. 3.

The best tomographic plane for the CBD in 40 children of different ages.

PROLONGED INFUSION CHOLANGIOGRAM

Table I gives details of the eight patients who proceeded to prolonged infusion cholangiography because the standard IVC was not diagnostic. The biliary tract was well shown in one case in which a standard IVC had failed to produce any opacification. There was improved opacification in two other cases leading to a diagnostic demonstration in one of them.

TOMOGRAPHY

Tomography was used in 40 examinations and in a similar proportion of cases in all age groups. In the prone position the CBD was demonstrated best in a plane either 4, 5, or 6 cm above the table top at all ages (Fig. 3). The 5 cm plane was best in 65% cases, the 4 cm plane in 28%, and these two planes included the best tomograph in about 90% of patients in all age groups.

DISCUSSION

For routine use the choice for contrast medium delivery is between a direct injection given over ten minutes (Scholz *et al.*, 1975) or an infusion over

30–60 minutes (Bell *et al.*, 1978). Berk and Clemett (1977) recently reviewed the adult literature and found that no single cholangiographic method for adults is universally accepted.

In adults, hand injection over ten minutes gives maximum opacification of the CBD 20 minutes sooner than a 30-minute infusion (Scholz *et al.*, 1975; Lake and Engelbrecht, 1976) while slower infusion results in greater delay but less reaction (McNulty, 1968). We supervise the whole examination in the Radiology Department and prefer the shorter examination for children who require constant nursing care and in whom the reaction rate is lower than in adults.

The best dosage of contrast medium for adults is also controversial. Current opinion favours the lowest dosage consistent with satisfactory results in order to minimize side effects (Ansell and Faux, 1973; Scholz *et al.*, 1974). Our results indicate that the dosage cannot be reduced below 100 mg iodine/kg in children without sacrificing diagnostic quality using the method described.

The incidence of side effects in adults varies greatly in different reports. In most large series there is an incidence of 10–14% with a ten-minute hand injection (Scholz *et al.*, 1975; Shehadi, 1975; Wise, 1973). Six percent of the patients in this series suffered possible side effects but this figure was exaggerated by the frequency of vomiting as a presenting symptom. Minor subjective sensations cannot be assessed in young children but reactions to cholangiographic media appear to be less frequent in the paediatric age group (Chaumont *et al.*, 1974; Fahr *et al.*, 1977).

Ioglycamate has a lower chemical toxicity than iodipamide but there is no evidence that it gives better opacification of the biliary tree. No practical differences in the time of maximum opacification or the quality of results emerged in our patients and the series was too small to compare the incidence of side-effects.

An exposure 45 minutes after commencing the injection gave maximum information of the CBD in over 80% of patients and the greatest number of ducts were best seen at this time. Scholz *et al.* (1975) found exposures at a similar time to be the most useful for the CBD in adults.

Fuchs and Preisig (1975) reported good results with the use of prolonged infusion cholangiography in adults after unsuccessful standard IVC but the method has not gained general acceptance. Chaumont *et al.* (1974) have used this method to show the gall bladder in neonates when endeavouring to distinguish neonatal hepatitis from biliary atresia. The examinations reported here following an infusion over 3–8 hours showed improvement of diagnostic value in two of eight cases. This suggests that prolonged infusion is of some value but that the returns are small for the longer procedure.

The biliary tree was satisfactorily demonstrated in a similar proportion in all age groups in spite of the small size of the CBD in young children, that is 4 mm or less in children under six years (Witcombe and Cremin, 1978). About 90% of bile ducts are seen in one of two tomographic planes in the prone position irrespective of age for the relatively large liver and 'pot-belly' of young children offset the larger general size of older children.

Demonstration of bile ducts by IVC is as successful in children as in adults and exposures can be made at a similar time after injection. The optimal tomographic plane is more readily achieved in children and the incidence of side-effects is less. A dosage of contrast medium containing approximately 100 mg iodine/kg (0.6 ml/kg Biligram injection or 0.4 ml/kg Biligrafin forte) is recommended when given by a ten-minute injection.

ACKNOWLEDGMENTS

The advice of Professor P. Folb, Department of Pharmacology, and Dr. R. Macdonald, Institute of Child Health, both of the University of Cape Town, is acknowledged. The statistical assistance of Dr. N. Wald, Department of the Regius Professor of Medicine, University of Oxford, is appreciated, and the assistance of the Medical Research Council of South Africa, is also gratefully acknowledged.

REFERENCES

ANSELL, G., and FAUX, P. A., 1973. Low-dose infusion cholangiography. *Clinical Radiology*, *24*, 95–106.

BELL, G. D., FRANK, J., FAYADH, M., SMITH, P. L. C., and KELSEY FRY, I., 1978. Ioglycamide (biligram) studies in man. Radiological opacification of the bile duct. A comparison of a number of different methods. *British Journal of Radiology*, *51*, 191–195.

BERK, R. N., and CLEMETT, A. R., 1977. *Radiology of the Gallbladder and Bile Ducts*. W. B. Saunders Co., Philadelphia, London and Toronto. Ch. 5.

CHAUMONT, P., KALIFA, G., and FONTAINE, Y., 1974. La cholangiographie par perfusion lente chez l'enfant. *Annales de Radiologie (Paris)*, *17*, 441–443.

CREMIN, B. J., and FISHER, R. M., 1976. Biliary ascariasis in children. *American Journal of Roentgenology*, *126*, 352–357.

FAHR, K., OPPERMANN, H. C., and WILLICH, E., 1977. Die Intravenöse cholangiocystographie im kindesalter. *Fortschritte auf dem Gebiete der Roentgenstrahlen*, *126*, 571–576.

FUCHS, W. A., and PREISIG, R., 1975. Prolonged drip-infusion cholangiography. *British Journal of Radiology*, *48*, 539–544.

GORDON, I. R. S., and ROSS, F. G. M., 1977. *Diagnostic Radiology in Paediatrics*, pp. 209 (Butterworths, London).

LAKE, W. T., and ENGELBRECHT, H. E., 1976. A clinical and radiological trial of meglumine ioglycamate. *South African Medical Journal*, *50*, 2007–2011.

MCNULTY, J. G., 1968. Drip-infusion cholangiography. *Radiology*, *90*, 570–575.

Nahum, H., Poree, C., and Sauvegrain, J., 1969. The study of the gallbladder and biliary ducts. *Progress in Pediatric Radiology*, 65–95. (Karger, Basel, New York, Chicago).

Reichelderfer, T. E., and Van Hartesveldt, J., 1955. Intravenous cholecystography with cholegrafin in infants. *American Journal of Disease of Children, 59*, 591–595.

Scholz, F. J., Johnston, D. O., and Wise, R. E., 1974. Hepatotoxicity in cholangiography. *Journal of the American Medical Association, 229*, 1724.

Scholz, F. J., Johnston, D. O., and Wise, R. E., 1975. Intravenous cholangiography. *Radiology, 114*, 513–518.

Shehadi, W. H., 1975. Adverse reactions to intravascularly administered contrast media. *American Journal of Roentgenology, 124*, 145–152.

Wise, R. E., 1973. In *Alimentary Tract Roentgenology*. pp. 1292, Ed. A. R. Margulis and H. J. Burhenne, (C. V. Mosby, St. Louis).

Witcombe, J. B., and Cremin, B. J., 1978. The width of the common bile duct in childhood. *Pediatric Radiology, 7*, 147–149.

Book reviews

Textbook of Nuclear Medicine: Basic Science. By A. F. G. Rocha and J. C. Harbert, pp. xix+412, 1978 (London, Henry Kimpton Publishers), £19·25.
ISBN 0-8121-0630-X

The first eight chapters of the book deal with the physics of radioactivity, detection of radiation, statistics of counting and radiation safety. More comprehensive description than normal is given to the production of radionuclides, generator systems, chemistry and quality control of radiopharmaceuticals, then the tools of nuclear medicine—scanners, cameras—are explained. The treatment of computer systems and whole body counters is brief. A chapter is devoted to each of ultrasound and computerized tomography and the book closes with four chapters on radioimmunoassay, radio-microbiology, labelled carbon breath analysis and *in vivo* neutron activation. Whether all this is, or is going to be, part of nuclear medicine is debatable; knowledge of competitor's methods is still useful.

The style is informal, maybe too much so, and this combined with the mistakes—factual and typographical—which abound in the first half of the book creates the impression that the science of nuclear medicine is not an exact one. A good textbook gives instruction in a logical and methodical manner, building on and referring to previous information. This book is a collection of essays with repetitions (graphs of linear absorption coefficients are provided four times, once wrong) and omissions (SI units are mentioned on p. 149, even there the becquerel is abbreviated to Bk). A successful textbook is reliable and authoritative—this one, sadly, is not such a book. Thirty-two contributors from North and South America produced the 22 chapters and neither authors nor editors spent enough time to check the text. The chapter of counting statistics is a good example of the mis-statements, printing errors, arithmetical errors leading to wrong conclusions (*e.g.* p.78 $\sqrt{12{,}000/3+11850/3}=\mathit{89.2}$ not 62.8 therefore $\tau=\mathit{1.68}$ not 2.4 therefore the counting difference of 150 could occur by chance with 10% probability which is *not* significant.

This book cannot therefore be recommended to students or practitioners of nuclear medicine.

K. F. Szaz.

Pediatric X-ray Diagnosis. By John Caffey, 7th edn., Vol. 1, pp. 1–976, Vol. 2, pp. 977–1844, 1978 (Year Book Medical Publishers Inc. London), £74·50.
ISBN 0-8151-1427-3

Dr. Caffey did not live to see the 7th edition of his monumental text book in print; sadly he died before its publication, but after the manuscript had been completed, and he was able to contribute his own preface to the edition. No man could wish for a finer memorial to his name. Some proper nouns have entered the English language as generic terms: just as "Mackintosh" has become synonymous with "raincoat", so has "Caffey" almost come to stand for a textbook of paediatric radiology.

The virtues of the previous editions are well known and the new edition lives up to its predecessors. New imaging techniques are included; there is now some mention of computerized tomography and of isotope and ultrasound scanning where that is helpful. Many new observations have been included and illustrations added. For instance, Dr. Caffey states in his preface that in the section on the skeleton there are 449 new insertions and deletions and 439 new references. This has added approximately 250 pages, bringing the work to something over 1800 pages in two volumes. Unfortunately the cost has gone up to £74, compared with £33·50 for the 1972 edition. It must be admitted that the production is extremely handsome: binding and paper are of the highest quality, and for once the reviewer has no grumbles concerning the reproduction of the radiographs. These are of uniformly high standard.

The present two volumes are clearly too large as preparation for an examination, but are by far the best reference work of paediatric radiology in the English language. I suspect that College visitors when assessing the departmental libraries of training departments, will want to see a fairly recent edition of "Caffey" included—best of all this 7th edition. I would certainly not like to be without it. One may hope that Dr. Caffey's associates in the writing of this book will continue to revise and bring it up to date from time to time, and so keep the name of a great radiologist alive amongst us.

F. Starer.

1979, *British Journal of Radiology*, *52*, 458–460

Traumatic para-mediastinal air cysts

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(*Received September, 1978*)

ABSTRACT

Two cases of traumatic para-mediastinal air cyst are presented. The air and fluid collection develops between two layers of the pulmonary ligament following trauma to the lung and rupture of alveoli adjacent to the pulmonary ligament.

Two cases of traumatic para-mediastinal air cysts, following blunt chest trauma are presented. The cysts appear to be a result of rupture of alveoli adjacent to the pulmonary ligament. Accumulation of blood in addition to air resulted in the production of an air fluid level.

CASE REPORTS

Case 1

On June 15, 1975, a 16-year-old white boy riding a motorcycle, veered into a ditch, was thrown from the motorcycle and landed on his abdomen. That evening he was short of breath and nauseated. He was brought to the Emergency Room by his parents on the morning of June 16, 1975. Physical examination showed several abrasions and small lacerations on his face. The remainder of the physical examination was essentially unremarkable.

A chest radiograph showed a collection of air with a fluid level in the left para-mediastinum (Fig. 1A). A barium swallow was normal (Fig. 1B). The patient tolerated a regular diet with no urinary or gastrointestinal symptoms. There were no respiratory symptoms and the patient was discharged after 10 days with no specific therapy. The para-mediastinal air cyst had completely cleared after approximately two weeks.

Case 2

A 14-year-old male fell 25 feet from an apple tree. He was unconscious for an unknown period of time. Upon awakening he vomited three times with small flecks of blood in his vomitus.

A nasogastric tube was inserted and there was a small amount of bright red blood in the aspirate. The haemoglobin and haematocrit remained stable. Physical examination showed no abnormality.

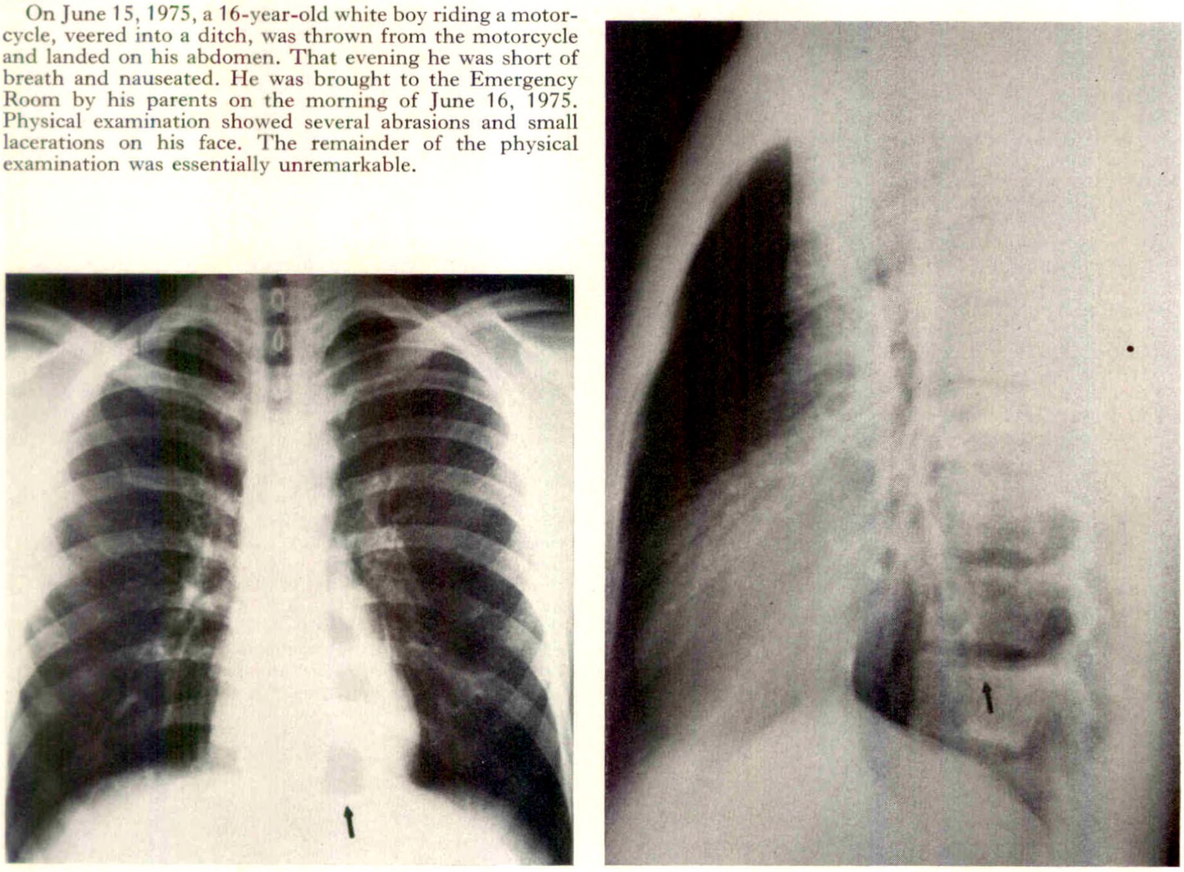

FIG. 1A.

AP and lateral chest roentgenographs showing traumatic left para-mediastinal air cyst. In lateral view the air fluid level over lower dorsal spine is seen. (Solid arrow).

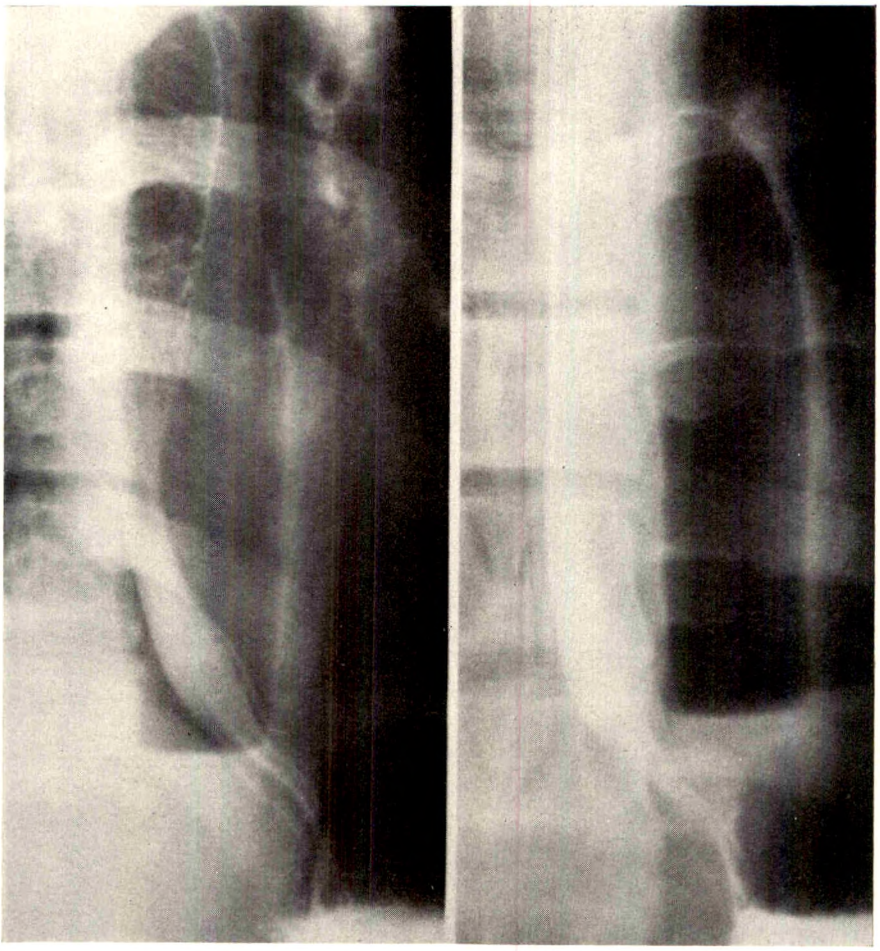

FIG. 1B

Barium swallow showed no evidence of extravasation and triangular traumatic air cyst with air fluid level again showed clearly.

Chest and abdominal radiographs obtained in the Emergency Room a few hours after trauma showed an air collection in the para-mediastinal region with an air fluid level (Fig. 2). The patient's condition remained stable and the day after admission he was discharged.

DISCUSSION

Both cases have similar radiographic findings. The interesting point about them is the consistency in the shape and location of the air fluid collection in the left para-mediastinal region. These two cases also correspond with previously reported cases by Hyde (1971) which showed air loculated in the left pulmonary ligament.

Para-mediastinal air cyst formation is presumably due to pulmonary laceration adjacent to the pulmonary ligament allowing air to escape between the two layers of the ligament. Blood may accumulate within the cyst due to rupture of capillaries of the lacerated alveoli.

The entity of traumatic para-mediastinal air cyst was described by Hyde (1971) who presented two patients. Our cases also followed trauma and the lesions disappeared spontaneously. The pulmonary ligament was described in detail by Rabinowitz and Wolfe (1966). It consists of two layers of serosal connecting the viseral pleura on the mediastinal surface of the lower lobe of each lung to the parietal pleura covering the mediastinum. This ligament forms a barrier between the anterior and posterior parts of the portion of the pleural cavity below the root of the lung. In normal persons it is not seen on radiographs. When it is stretched to its maximum size the ligament has a triangular appearance.

The air-fluid collections in our cases correspond

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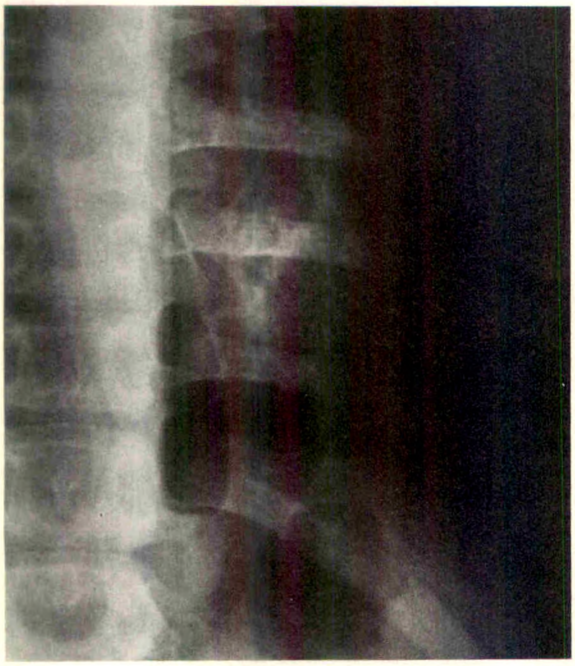

FIG. 2.

AP chest X-ray following admission shows a triangular left para-mediastinal air cyst with air fluid level.

anatomically to the pulmonary ligament. The air may have no connection with the pleural cavity and will be absorbed within a few days. It is of interest that para-mediastinal air cysts have only been noted on the left side of the chest. The reason for this is not clear. Anatomically there is no significant difference between the left and right pulmonary ligament, except that the left lies adjacent to the oesophagus anteriorly and is bounded posteriorly by the descending aorta and the right is related anteriorly to the inferior vena cava and posteriorly to the azygos vein.

The para-mediastinal air cyst does not change in position, whereas a pneumothorax might be seen to move to the apical region. With a pneumomediastinum the air will extend into the soft tissues of the mediastinum and neck, and the pulmonary ligament will not be outlined.

REFERENCES

HYDE, I., 1971. Traumatic para-mediastinal air cyst. *British Journal of Radiology*, *44*, 380–383.

RABINOWITZ, J. G., and WOLFE, B. S., 1966. Roentgen significance of the pulmonary ligament. *Radiology*, *87*, 1013–1020.

Book review

Medical Physics. By J. R. Cameron and J. G. Skofronick pp. xvii+615, illus., 1978 (John Wiley and Sons, New York), £15·50.
ISBN 0-471-13131-8.

This is an unusual book. It is different from the majority of books on medical physics because, in the authors' words, it is written primarily for students who plan to make a career in some field of medicine.

The authors describe the way in which physics can be used to understand the structure and function of the human body. The necessary physiology and anatomy, at an introductory level, is described simply and clearly, along with the ways in which physics can be used to measure and study the behaviour of the body. At the same time, the use of quantitative methods in the assessment of abnormal or diseased conditions is described.

The book is very suitable as a text for medical students with an understanding of elementary physics. It is also, because of its wide coverage of subjects, of interest and value to practising medical physicists. For example, the application of the SQUID (superconducting quantum interference device), which will detect a steady or alternating magnetic field of 10^{-9} times the earth's field, to record the magnetic field near the heart is described and illustrated.

The authors have not overlooked the more common applications of physics in medicine, and there are chapters dealing with diagnostic X rays, nuclear medicine, radiation therapy and radiation protection; each chapter provides an excellent introduction to its topic.

All in all, a fascinating and interesting book for the practising hospital physicist; for someone who is involved in teaching, an invaluable reference book.

N. W. RAMSEY.

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Kidney distension during IV urography in normal rats and in rats with artificial unilateral renal artery stenosis

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(*Received December, 1978*)

ABSTRACT

Acute changes in kidney size during IV urography were studied in normal rats and in rats with artificial unilateral renal artery stenosis. In normal rats, IV bolus injection of sodium iothalamate (400 mg I/ml), 1.5 ml/kg body weight, produced an increase in area of the renal silhouette by an average maximum of 12.7% after 60 seconds. In nine out of ten rats which developed hypertension after left sided renal artery clamping, renal distension was either small or absent on the stenosed side, while the contralateral right kidney showed normal distension during IV urography. Two out of three rats, which remained normotensive after renal arterial clamping, showed normal distension of both kidneys.

These results confirm earlier observations in man that the acute changes in size of the kidney during IV urography can be used as an aid in the urographic screening of hypertensive patients for significant renal arterial stenosis.

In all rats with arterial clamp and hypertension, the stenosed kidney was smaller than its contralateral mate. An index between the size of the non-stenosed and the stenosed kidneys ≥1.15 was only seen in these particular rats.

It is well known that kidney size increases during IV urography (Wolpert, 1965; Arkless, 1969). By addition of a diuretic ("vasodilated excretory urography", washout urography) renal distension will be enhanced and can be demonstrated by measuring the area of the renal silhouette directly on the radiographs (Wolf and Wilson, 1972; Dorph and Øigaard, 1973a). It has been shown in man that diminished or abolished renal distension indicates the presence of a significant renal artery stenosis (Dorph and Øigaard, 1973b; Wolf, 1973).

In the present work this clinical observation has been tested in the experimental animal. The renal distending effect of an intravenous bolus of water-soluble radiographic contrast medium was studied in the normal rat and in rats with artificial unilateral renal artery stenosis.

MATERIAL AND METHODS

White Wistar rats weighing between 220 and 350 g were examined. After 12 hours fasting they were anaesthetized with pentobarbital 0.8–1.2 mg intraperitoneally. Additional pentobarbital in doses of 0.2 mg was given as needed to maintain anaesthesia. A polyethylene catheter (0.3 mm inner diameter) was placed in the jugular vein by cut down and flushed with heparinized saline. The rat was fixed in the dorsal recumbent position on a thin wooden plate. Magnified (5 times) radiographs of the kidney region were obtained on a film changer before and 5, 15, 30, 60, 120, 180, 240 and 300 seconds after starting rapid (one second) bolus injection of sodium iothalamate (400 mg I/ml), 1.5 ml/kg body weight, through the jugular catheter.

The outer contour of the kidney shadow was delineated with a pencil directly on the radiographs. A straight line was drawn between the medial contours of the upper and lower poles. The circumscribed area of the kidney shadow was determined by repeated planimetry as described earlier (Dorph and Øigaard, 1973a).

The absolute values of kidney area on the magnified radiographs were about 20 cm^2. Since the renal shadow could often not be delineated with sufficient accuracy on the scout film, the five second film was used as zero value. On this exposure the contour of the kidney was always clearly visible.

An index of the relative size of the two kidneys was calculated as $\frac{\text{area of right kidney}}{\text{area of left kidney}}=\text{size index}$. The five second film was used for these measurements. 12 normal rats and 13 rats with artificial unilateral renal artery stenosis were examined.

Renal artery stenosis

The operative procedure had been carried out from three to seven (average 4.8) weeks prior to the examination. During laparotomy a silver clamp was applied on the left renal artery aiming at reducing the diameter of the vessel by about 50%. Blood pressure was measured regularly during the postoperative phase using a photoelectric sphygmomanometric device on the tail of the conscious rat. This method provides reproducible blood pressure values very close to the animal's systolic blood pressure (Palbøl and Henningsen, 1979).

RESULTS

Ten rats developed hypertension (systolic blood pressure ≥150 mm Hg), average 176 mm Hg (150–220 mm Hg) after the operation. Three rats remained normotensive in spite of the arterial clamp with systolic blood pressures of 120, 120 and 125 mm Hg.

Normal rats

Changes of kidney size during the first five minutes following IV bolus injection of contrast medium for the 24 kidneys examined are given in Fig. 1. Prompt renal distension was observed as early as 15 seconds, reaching a maximum after two minutes. After five minutes there was a slight, but significant decrease in size. Average distension after two minutes was 12.7% (SD 4.5). In no case was the measured area increase less than 7%. The average size index was 1.025 (range 0.98–1.11, SD 0.038).

Rats with unilateral artery clamp

a. *Hypertensive rats.* As appears from Fig. 2, nine of the ten hypertensive rats showed maximum distension of the stenosed kidney of less than 5% during urography. The average distension after two minutes was 2.2% (0.7–3.8%). One rat with a systolic blood pressure of 220 mm Hg showed considerable distension of the stenosed kidney (18.3%). The size index varied between 1.15 and 2.69 (average 1.52, SD 0.48).

b. *Normotensive rats.* Figure 2 also demonstrates that two of the three rats, which did not develop hypertension after arterial clamping showed normal distension of the affected kidneys. Their size indices were 1.05 and 0.99 respectively. One rat with systolic blood pressure 120 mm Hg showed a 4% distension of the stenosed side. Its size index was 1.15.

All *contralateral kidneys* showed distension within the normal range (9–19%).

Two of the rats were examined both before and after the application of the arterial clamp and thus constitute part of both the normal and the operated

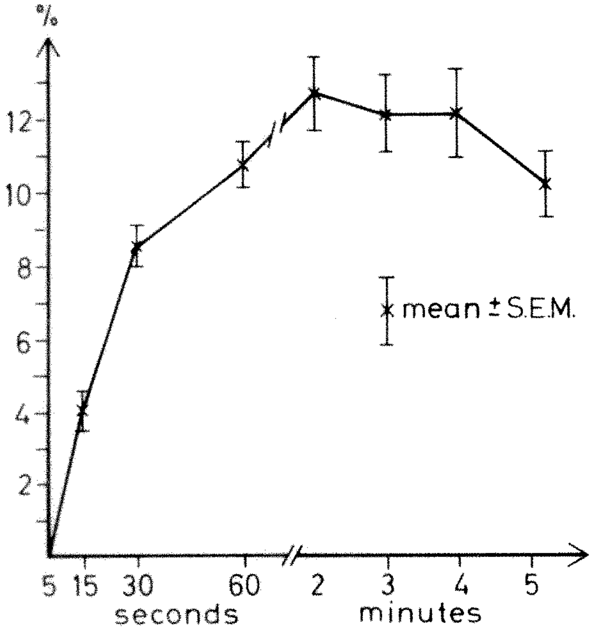

FIG. 1.

Changes in area of kidney shadow (per cent) during the first five minutes after intravenous bolus injection of sodium iothalamate (400 mg I/ml), 1.5 ml/kg body weight, in 12 normal rats (24 kidneys).

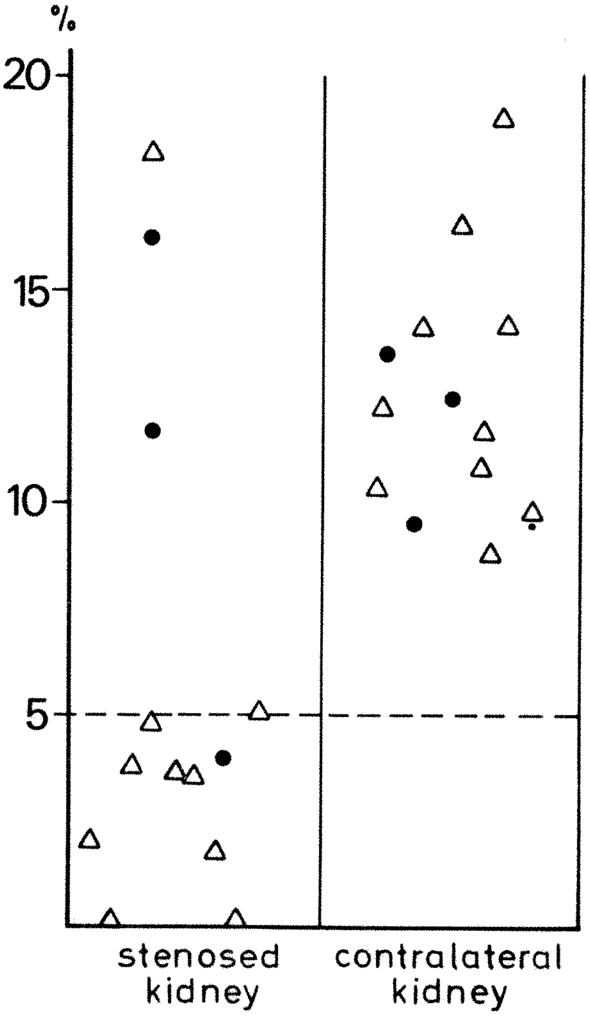

FIG. 2.

Distension of stenosed and contralateral kidneys during intravenous urography in 13 rats with artificial unilateral renal artery stenosis. △=hypertensive rats, ●=normotensive rats. (Per cent change in area of renal silhoutte.)

material. One developed hypertension, the other remained normotensive after application of the clamp. Both rats showed distension of less than 5% of the stenosed kidney after the operation, and their size index changed from 1.03 and 1.01 to 1.20 and 1.15, respectively.

Discussion

The acute effects of radiographic water-soluble contrast media on kidney size were first described by Wolpert (1965). Since then it has been demonstrated by several investigators that contrast media in doses usually employed for IV urography cause a prompt increase in kidney size. By the addition of diuretics, the renal distending effect can be enhanced and quantitated in clinical practice by measuring the area of the renal silhouette directly on the radiographs. A small initial renal shrinkage, which has been demonstrated in the dog (Cramer and Hegedüs, 1977; Dorph *et al.*, 1977) was not observed in the present experiments, possibly because it occurred too rapidly to be demonstrated with the technique used. The relatively high cardiac output in these small animals probably also accounts for the more rapid distension of the kidney. By contrast medium alone, the average increase in area of the renal silhouette was 12.7%, which is considerably higher than seen in man (Dorph and Öigaard, 1973a) and in the dog (Dorph *et al.*, 1977). Also, Hegedus *et al.* (1978) found the volume variations of the rat kidney in response to contrast media to be relatively greater than in the man and dog. In any case, the increase was of an order of magnitude which could be readily demonstrated without the addition of a potent diuretic.

Wolf (1973) has suggested that kidney distension following IV contrast medium injection is caused by renal vasodilation. However, experimental investigations by Dorph *et al.* (1977) and by Hegedüs *et al.* (1978) indicate that the mechanism is rather a distension caused by the substantial osmotic diuretic effect of the media.

Decreased or abolished kidney distension during "vasodilated excretory urography" or washout urography as a sign of significant renal arterial stenosis has been demonstrated in small groups of patients (Dorph and Øigaard, 1973b; Wolf, 1973). However, the practical value of these measurements has been questioned (Talner *et al.*, 1978), and the final evaluation must rest on larger series, which—for obvious reasons—can only be achieved from cooperative studies running for years. There are still several factors of uncertainty regarding the final diagnosis in each individual case (Dorph, 1976).

Some of these problems have been overcome when working with the experimental animal as in the present study, where the application of an arterial clamp and postoperative observation of the arterial blood pressure establishes the causal connection between the stenosis and the hypertension. Results of the present study are in good agreement with the clinical observation that lack of renal distensibility is a good, although not infallible, indicator of significant renal arterial stenosis, and that it can be used as a supplement to the urographic evaluation of hypertensive patients whenever the quality of the urogram allows such measurements. As the only urographic sign not based upon a side difference, it is of special value in cases of bilateral stenosis.

In the present experiments an index between the size of the non-stenosed and the stenosed kidney $\geqslant 1.15$ was shown to be just as reliable an indicator of significant stenosis. However, this is certainly not the case in the clinical situation, where several factors may influence the relative size of the two kidneys.

REFERENCES

Arkless, R., 1969. The normal kidney's reaction to intravenous pyelography. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 107*, 746–749.

Cramer, B. M., and Hegedüs, V., 1977. Relationship between renal lymph flow and changes in kidney size during urography. *Investigative Radiology, 12*, 251–255.

Dorph, S., 1976. Intravenous urography in the diagnosis of renovascular hypertension. *Danish Medical Bulletin, 23*, 12–23.

Dorph, S., Sovak, M., Talner, L. B., and Rosen, L., 1977. Why does kidney size change during IV urography? *Investigative Radiology, 12*, 246–250.

Dorph, S., and Øigaard, A., 1973a. Variations in size of the normal kidney following intravenous administration of water-soluble contrast medium and urea. *British Journal of Radiology, 46*, 183–186.

Dorph, S., and Øigaard, A., 1973b. Variations in renal size in the diagnosis of renovascular hypertension. *British Journal of Radiology, 46*, 187–190.

Hegedüs, V., Faarup, P., Nørgaard, T., and Lønholdt, C., 1978. Volume changes in the rat renal cortex during urography. *British Journal of Radiology, 51*, 793–798.

Palbøl, J., and Henningsen, J., 1979. Blood pressure measurements in the conscious rat. *Scandinavian Journal of Urology and Nephrology*. (in press.)

Talner, L. B., Stone, R. A., Coel, M. N., Levy, S. B., and Emarine, C. W., 1978. Furosemide augmented intravenous urography: results in essential hypertension. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 130*, 257–260.

Wolf, G. L., 1973. Rationale and use of vasodilated excretory urography in screening for renovascular hypertension. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 119*, 692–700.

Wolf, G. L., and Wilson, W. J., 1972. Vasodilated excretory urography—an improved screening test for renal arterial stenosis? *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 114*, 684–689.

Wolpert, S. M., 1965. Variations in kidney length during the intravenous pyelogram. *British Journal of Radiology, 38*, 100–103.

1979, *British Journal of Radiology*, *52*, 464–467

Doppler ultrasound examination of pathologically enlarged lymph nodes

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ABSTRACT

Pathologically enlarged lymph nodes have been examined with a commercially available 10 MHz continuous-wave Doppler flowmeter. Many enlarged lymph nodes gave rise to significant Doppler-shift signals indicating increased blood flow. The signals have been spectrum analysed and the large diastolic flow components suggest that there is considerable arterio-venous shunting within lymph glands involved in leukemia, lymphoma and carcinoma. It also seems that the signals tend to diminish in response to treatment. The Doppler signals have been used in an imaging system to produce a vascular map of the region of the enlarged gland. It is suggested that these findings might be applicable to the detection of neoplastic tissues in less accessible sites.

Ultrasonic Doppler flowmeters are readily available and cheap. They provide a transcutaneous means of detecting movement of structures and tissues within the body. They are in common diagnostic use for the detection of the fetal heart from the eighth week of gestation onwards and find application in the diagnosis of deep vein thrombosis. Doppler flowmeters are also being used to monitor blood-flow characteristics at various sites in the body (Wells, 1977).

Recent work at this centre has demonstrated that abnormal Doppler signals originating from breast carcinomas are helpful in distinguishing benign and malignant lumps in the breast (Wells *et al.*, 1977). The present study was undertaken to investigate whether similar signals were associated with other neoplastic tissues. The equipment used was a commercially available Doppler flowmeter* operating at an ultrasonic frequency of about 10 MHz. The use of such a high ultrasonic frequency tends to improve the sensitivity of the technique since the echo backscattered by blood increases as the fourth power of frequency (Shung *et al.*, 1976). However, 10 MHz ultrasound is attenuated rapidly in human tissue, limiting the useful range to about 30 mm. Neoplastically enlarged superficial lymph nodes were therefore chosen as suitable objects for study since they are readily accessible to ultrasonic investigation and, furthermore, are frequently biopsied, providing an exact histological diagnosis.

MATERIAL AND METHOD

Forty-one patients with palpable lymph glands were investigated. Most cases involved the axillary cervical or supraclavicular glands. The region under investigation was liberally coated with oil and the ultrasonic transducer moved over the skin surface. The audio output of the Doppler flowmeter was monitored by two independent observers with individual headsets. In addition, signals were recorded on magnetic tape for subsequent spectrum analysis using a Kay Sonograph (model 6061B).† Signals were obtained from the region of the enlarged gland and attempts were also made to trace out the courses of surrounding arteries and veins. Comparisons were made between corresponding areas on the two sides of the body.

Arteries and veins give rise to readily recognizable Doppler signals: veins are associated with a continuous "rushing" sound which can often be modulated by respiration; arteries produce a sharply pulsatile signal. A typical sonograph from a jugular vein is shown in Fig. 1a. It can be seen that the Doppler frequencies are constant over the cardiac cycle corresponding to the steady flow of blood through the venous vessel. In contrast Fig. 1b is a typical carotid artery sonogram showing the rapidly rising velocities during systole, which fall rapidly away and oscillate during diastole. The Doppler signals detected in the region of pathologically enlarged lymph nodes were frequently found to be abnormal spatially and qualitatively.

Spatial abnormalities

Doppler signals of arterial or venous type were generally found arising from, or adjacent to, the lymph gland. These signals, when compared with the contralateral site, did not correspond to normal vascular structures of the neck or axilla. The distinction from normal was sometimes difficult where glands were clustered around major vessels. It is suggested that this type of signal probably arose from abnormal feeding and draining vessels supplying the enlarged lymph node.

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*Model 806 Parks Flowmeter, Parks Electronics Laboratories, Beaverton, Oregon, USA.

†Kay Elemetrics Co., Pine Brook, New Jersey, USA.

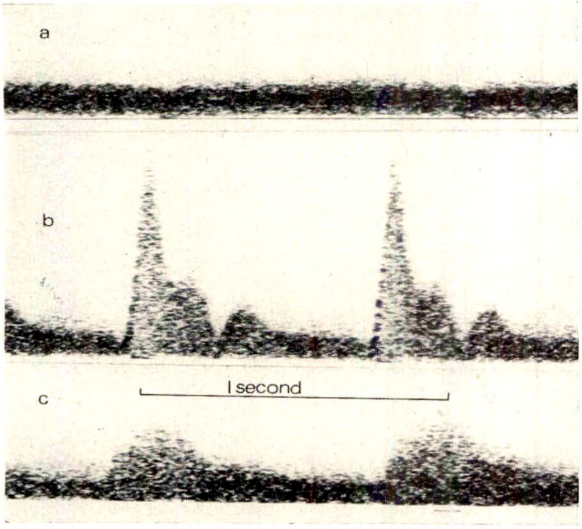

FIG. 1.

Typical sonograms from: (a) jugular vein; (b) carotid artery; (c) enlarged lymphomatous gland. Time is displayed horizontally and Doppler frequency (corresponding to blood velocity) vertically. The degree of blackening indicates the amount of blood flowing at the particular velocity and time.

Qualitative abnormalities

In a minority of cases, the glands themselves gave rise to a "characteristic" Doppler flow signal. A sonogram of such a signal (which is readily recognized by the trained human ear) is shown in Fig. 1c. It is generally lower pitched and less pulsatile than an arterial signal, with a slow systolic rise and a gradual fall into diastole. It is suggested that this type of signal probably arises from arterio-venous shunting within the gland.

In an attempt to develop a more objective approach to the investigation, a Doppler scanning technique similar to that described by Reid and Spencer (1972) was used to image the vasculature in the region of the gland. The transducer was mounted on a scanning arm so that its position could be monitored and mapped onto an oscilloscope screen. It was also arranged that a spot was written onto the screen at a position corresponding to the location of the transducer whenever a Doppler signal at a significant frequency was detected. Thus, by moving the transducer over the skin surface, a plan view of the vascular structures in the region of the lymph glands was obtained. A typical scan of the right side of the neck is shown in Fig. 2. It can be seen that the abnormal signals detected are remote from normal vascular structures and coincide with the palpable structure of the lymph gland.

TABLE I

SUMMARY OF RESULTS

	ABNORMAL DOPPLER SIGNALS		
	ABSENT	WEAK	STRONG
C.L.L.		●	● ● ● ● ●
LYMPHOMA	●	○ ○ ○ ○	○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○
CARCINOMA	● ● ● ●	● ● ○ ○ ○	● ● ● ○
BENIGN	○ ○ ○ ○		○ ○

● TREATED
○ UNTREATED

RESULTS

The results are summarized in Table I. Patients with chronic lymphatic leukemia (CLL), with only one exception, produced large amplitude, clearly abnormal Doppler signals which were often of the "characteristic" type. In this centre, most cases of CLL are aggressively treated with combination chemotherapy. Thus it seems that when palpable lymph nodes remain, they give rise to strong Doppler signals despite treatment.

Sixteen cases of lymphomatous enlargement were investigated. Most of the patients gave clearly abnormal Doppler signals, the only negative case being a non-Hodgkins lymphoma undergoing very rapid clinical regression in response to combination chemotherapy. Five of these cases have been re-examined after commencement of therapy and the abnormal signals have been observed to diminish and may disappear before the glands become impalpable.

Thirteen cases of lymph nodes invaded by metastatic carcinoma were investigated. These deposits gave rise to Doppler signals with a range of intensities. In general, however, it would seem that the signals from secondary carcinomas were of smaller amplitude and less clearly abnormal than those found in CLL and in lymphomas. However, this finding may be related to the fact that nine out of these 13 subjects had received local radiotherapy. No untreated cases failed to give rise to abnormal signals although the number in this category is very small.

No clear pattern has yet begun to emerge which links the form of the signal with the histology of lymphoma. Furthermore, it was expected that small well vascularized lymph nodes might give more intense signals than large partially necrotic ones, but as yet there appears to be no definite indication that this is the case.

Six patients with non-malignant lymph node enlargement were examined. Four cases showed an absence of any signal indicating blood flow. This group comprised two nodes with acute cervical lymphadenopathy following tonsillitis and two patients with chronic reactive axillary lymph nodes

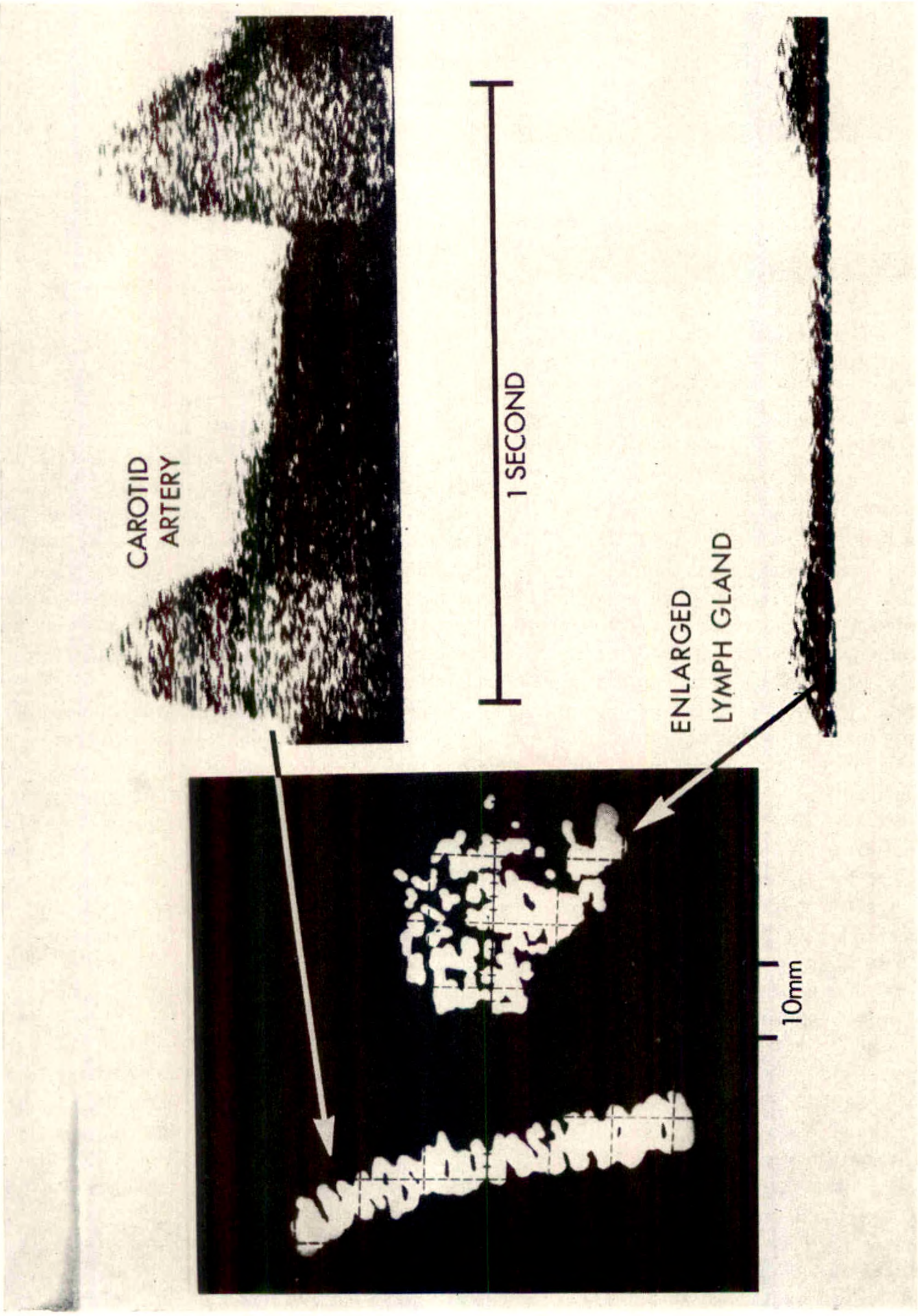

FIG. 2.

Doppler scan of right side of neck. Points of significant flow are shown white.

of many years standing. Two patients were encountered with strong Doppler signals localized to non-malignant glands. One case had a mass of grossly-inflamed tuberculous cervical glands and the other presented with a peculiar benign chronic lymphadenopathy. This was characterized pathologically by enlarged blood vessels running radially through the gland in a so-called "angiolymphomatous malformation."

DISCUSSION

Little is known about the blood supply to pathologically enlarged lymph nodes. The present study demonstrates that neoplastic enlargement is associated with increased vascular signals. In addition, a distinctive signal is sometimes localized to the lymph gland itself and is possibly due to arterio-venous shunting. In theory, a "characteristic" signal would be expected from an elastic vascular structure with narrow feeding arteries (to give a slow rise time) supplying a low resistance periphery (giving a gradual decay of flow into diastole). Similar characteristic signals have been observed in breast carcinomas. Recent work suggests that formation of new vessels is crucial to the growth of neoplastic cells. It has been postulated that an hormonal substance known as tumour angiogenesis factor stimulates this growth (Folkman *et al.*, 1971). As tumours enlarge, active division may become localized to a circumferential well-vascularized layer, while the centre becomes relatively avascular and necrotic.

The results presented here suggest that these vascular events may be detected using a sensitive Doppler technique. At present, it seems that this finding remains perhaps an interesting observation of arguable clinical value. However, it raises the possibility that Doppler signals may be used to enhance tumour detection in less accessible sites, for example within the abdomen.

At this centre, a conventional B-scan imaging system has been combined with a pulse-Doppler device (Atkinson and Wells, 1977). The B-scan provides a pulse-echo tissue map so that any ultrasonically-accessible point of interest can be interrogated for movement or blood flow using the pulse-Doppler attachment. This technique has found clinical application in distinguishing dilated bile ducts from vascular structures in the livers of jaundiced patients (Loh *et al.*, 1978). Preliminary work with this apparatus suggests that vascular signals can also be detected from pancreatic carcinomas, although hepatic metastases tend to be silent. More sensitive apparatus is now being developed for this type of investigation. Meanwhile, it has been found here that abdominal tumours do not give detectable signals when using the 10 MHz CW Doppler device. This is possibly because the high frequency of the ultrasound limits the penetration to about 30 mm since most of the energy is attenuated in the anterior abdominal wall. To overcome this problem, a catheter-tip probe has been devised which can be passed down the biopsy channel of a laparoscope. It is intended to place this in direct contact with liver metastases under direct vision at laparoscopy. If it is discovered that Doppler signals can be detected in this way, this should encourage further development of pulse-echo/Doppler hybrids working from the skin surface.

Many difficulties remain. Inflamed tissues are intensely vascular and it is unlikely that they could accurately be distinguished from neoplastic deposits solely by Doppler examination. Similarly, many malignant tumours are relatively avascular at angiography. However, the present observations encourage the authors to believe that Doppler techniques might improve and complement the already impressive role of conventional ultrasonic techniques in the detection of abdominal tumours.

REFERENCES

ATKINSON, P., and WELLS, P. N. T., 1977. Pulse-Doppler ultrasound and its clinical application. *The Yale Journal of Biology and Medicine*, *50*, 367–373.

FOLKMAN, J., MERLER, E., ABERNATHY, C., and WILLIAMS, G., 1971. Isolation of a tumour factor responsible for angiogenesis. *The Journal of Experimental Medicine*, *133*, 275–288.

LOH, C. L., ATKINSON, P., and HALLIWELL, M., 1978. The differentiation of bile ducts and blood vessels using a pulsed Doppler system. *Ultrasound in Medicine and Biology*, *4*, 1.

REID, J. M., and SPENCER, M. P., 1972. Ultrasound Doppler technique for imaging blood vessels. *Science*, *176*, 1235–9.

SHUNG, K. K., SIGELMAN, R. A., and REID, J. M., 1976 Scattering of ultrasound by blood. *I.E.E.E. Transactions on Biomedical Engineering BME–23*, *6*, 460/467.

WELLS, P. N. T., 1977. In: *Biomedical Ultrasonics*, chapter 7 (Academic Press, London).

WELLS, P. N. T., HALLIWELL, M., SKIDMORE, R., WEBB, A. J., and WOODCOCK, J. P., 1977. Tumour detection by ultrasonic Doppler blood-flow signals. *Ultrasonics*, *15*, 231–232.

1979, *British Journal of Radiology*, *52*, 468–471

The effect on dosimetry of changing from the lithotomy to the supine position in treating uterine cancer with the Cathetron and external radiotherapy

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ABSTRACT

Uterine carcinoma can be treated by combined external and intracavitary irradiation. With an afterloading technique intracavitary irradiation is given with the patient in the lithotomy position. External irradiation is given with the patient in the supine position. A lead shield is used with the external fields to cover the tissues which are close to the intracavitary sources and receive high doses. The positions of the intracavitary sources seen on radiographs taken when the patient is in the lithotomy position are transferred to films taken with the patient in the supine position. From the latter the position and profile of the shield are calculated. It is shown that a reliable transfer of the positions of the sources and determination of the necessary shielding cannot be achieved in this way. It is therefore concluded that both intracavitary and external irradiation should be carried out with the patient in the supine position.

Patients with uterine carcinomas can be treated by combined external and intracavitary irradiation. We have used an afterloading machine with high dose-rate sources (Cathetron) for intracavitary treatments. This technique was described in detail by O'Connell *et al.* (1967) and Joslin *et al.* (1972).

When the patient is in the lithotomy position the catheters are inserted into the vagina or the uterus. They are locked in this position during irradiation when the ^{60}Co sources are introduced into the far ends of the catheters. This is the most practical position for the procedure. External irradiation to the pelvis is given by anterior and posterior fields with the patient in the supine position. Tissues near to the far ends of the catheters receive a high dose from the intracavitary sources. In order to obtain an optimum dose in these tissues a lead shield is used in the external fields covering the central regions of the pelvis. The position and profile of this shield are calculated from radiographs taken during Cathetron treatments when the patient is in the lithotomy position. Another two pelvic radiographs are taken with the patient in the supine position simulating the conditions for external irradiation. The shielded areas calculated on the lithotomy films are then transferred to the supine films. Finally, the position and profile of this shield are drawn on the patient's skin.

The transfer of the area to be shielded is made using the pelvic bones seen on the films. If the pelvic girdle is stationary when the patient changes from the lithotomy to the supine position this transfer can be done easily, but this is seldom the case. Should the pelvic girdle of every patient rotate in a standard manner it might also be possible to make the transfer with satisfactory accuracy.

The effect of this rotation could be investigated by utilizing anatomical points on the pelvic girdle seen on the films. We have therefore studied how certain points move, as shown by the radiographs, when a patient changes position.

METHOD AND MATERIAL

Altogether 60 consecutive patients treated during the latter half of 1977 were studied. All had radiographs taken with the catheters inserted and locked in position. Both AP and lateral radiographs were taken with the patient in the lithotomy position. Immediately after this the legs were lowered gently to bring the patient into the supine position. Again AP and lateral films were taken. Extreme care was taken to prevent any change in the position of the catheters that were firmly locked in position from outside the pelvis. Three different points, A, B and C were selected on the film (Fig. 1). The lateral films were of varying quality so only AP films were utilized. The selected points were easy to define on all films used. Point A is at the upper limit of the symphysis. Point B lies on a line joining the upper limits of the two femoral heads. Point C lies on a line joining the upper limits of the major incisurae ichiadicae. All the points are in the same sagittal plane as the tip of the catheter. The distances between the three points and the tips of the catheters have been calculated for each patient. Altogether 26 patients had intravaginal catheters and 33 intrauterine.

Patients with endometrial carcinomas were subjected to hysterectomy and bilateral salpingo-oophorectomy. Those with carcinomas infiltrating the myometrium had six intravaginal Cathetron treatments. At each treatment they received a dose of 500 rad to a reference isodose line which passes

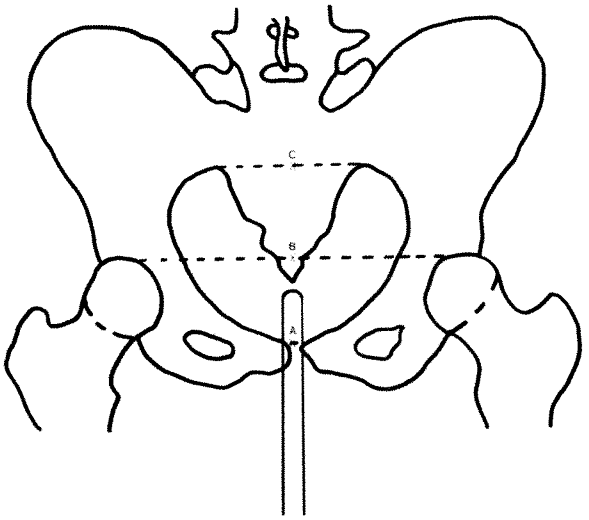

Fig. 1.

Points A, B and C were chosen because they could be found easily on all films and were located on the AP films. Point A is at the upper limit of the symphysis, B is on a line drawn from the upper limit of the two femoral heads and C on a line joining the upper limits of the major incisurae ischiadicae. The three points are on the same sagittal plane as the catheter tip.

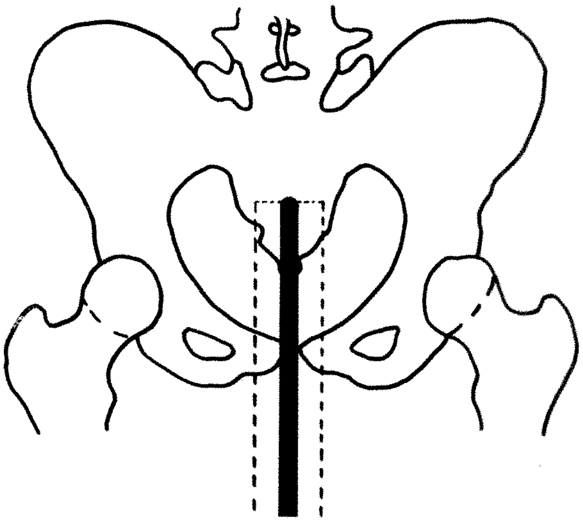

Fig. 2.

Position and profile of the shield in the external fields around the intracavitary catheter indicated by the dotted line.

through a point 1 cm from the surface of the catheter which receives the highest dose rate (Beckman, 1971). If a cylindrical Perspex applicator is placed round the catheter in the vagina the reference isodose will be through a point located 1 cm from the surface of the applicator. The intracavitary treatments were combined with external irradiation to the pelvis. This was given with a ^{60}Co unit or a betatron by anterior and posterior fields normally 16 × 16 cm. The patients first received 2000 rad to the whole pelvic region and then a further 2000 rad using a shield to cover the regions irradiated by the intracavitary sources. Normally one intravaginal and four external irradiations were given each week for a total time of about five weeks on average. The shields used were constructed to cover a region with a reference isodose curve of 500 rad around the catheters (Fig. 2). As the positions of the catheters at different treatments were not identical a mean reference isodose line was calculated.

Patients with intrauterine catheters usually had cervical carcinomas. They received five intracavitary treatments using one intrauterine and two vaginal catheters each time. The patients also received external irradiation by two opposing fields (16 × 16 cm) to the whole pelvis up to a total dose of 3000 rad. In addition they received a further 1500 rad using a lead shield which protected the area within a reference isodose line of 600 rad. When the shields were designed the positions of the vaginal catheters were considered but in this special study interest was concentrated on the position of the intrauterine catheter. The treatment period for each patient extended over about five weeks and each patient was given one intracavitary and four external irradiations weekly.

The distances between the three points A, B and C and the tip of each catheter were measured on each AP film to an accuracy of 1 mm. The films were taken under the same geometrical conditions when the patient was in the lithotomy or the supine position.

Two statistical analyses were performed. For each patient and for each point the difference between the measurements in the lithotomy and supine positions was calculated. The correlation and regression coefficients for paired case analysis were calculated according to the following formula (Armitage, 1973):

$$b=\frac{n\Sigma yx-\Sigma y\Sigma x}{n\,\Sigma x^2-(\Sigma x)^2} \qquad r_{xy}=b\frac{S_x}{S_y}$$

where y is the distance between the catheter tip and A, B and C with the patient in the supine position;

TABLE I

Differences of distances between three points on the radiographs and the catheter tip taken with the patients in the lithotomy and supine positions

Catheter position	Number of patients	Point on radiographs	Difference of distances between catheter tip and point (mm)		Significance of difference
			X̄	S.D.	
Intrauterine	33	A	12.6	12.2	XXX
		B	8.6	12.8	XXX
		C	0.9	15.3	N.S.
Vaginal	27	A	14.9	11.1	XXX
		B	0.22	18.1	N.S.
		C	1.9	11.8	N.S.

XXX = highly significant ($P < 0.001$); N.S. = not significant ($P > 0.05$).

TABLE II

Correlation and determination coefficients for the distances between three points and the catheter tip with the patients in the lithotomy and supine positions

Catheter position	Number of patients	Point on radiographs	r_{xy}	R^2
Intrauterine	33	A	0.84	0.71
		B	0.78	0.62
		C	0.70	0.50
Vaginal	27	A	0.77	0.59
		B	0.41	0.17
		C	0.71	0.50

r_{xy} = the correlation coefficient; R^2 = the determination coefficient of linear regression.

x is the distance between the catheter tip and A, B and C with the patient in the lithotomy position;
r_{xy} is the correlation coefficient;
S_x and S_y are standard deviations of x and y;
R^2 is the coefficient of determination where $R^2 = r_{xy}{}^2$.

Results

The hypothesis to be tested is that, on average, points A, B and C do not alter in position when a patient moves from the lithotomy to the supine position. This hypothesis was rejected for points A and B in the intrauterine catheter cases. No significant difference was found for point C. For the vaginal cases the hypothesis was rejected for point A. This was not so for points B and C (Table I).

Our results indicate that the mean distance from the catheter tip to point C did not alter when the patient moved from the lithotomy to the supine position. However, the standard deviations of the differences were large for all three points. Thus it was impossible to reach a reliable conclusion for individual patients.

The correlation between the distances with the patient in the lithotomy and supine positions can be seen in Table II. The coefficient was in no case large enough to permit a reliable calculation of the catheter position when the patient changed position. Nor did a regression analysis produce coefficients that were sufficiently reliable to permit prediction of the supine position, given the values for the lithotomy position.

Discussion

These results show that the distances between certain points related to the pelvis and the catheter tips changed when the legs of patients were moved. There were also great variations for all of the distances. When intracavitary irradiation was given with the patient in the lithotomy position no reliable prediction could be made about the position of the sources in the pelvis when the patient received external irradiation in the supine position. This means that the profile and position of the lead shield in the external fields cannot be predicted with reliable accuracy by using this method.

Therefore the technique was changed. The intracavitary catheters are now inserted with the patient in the lithotomy position. Then the legs are lowered carefully to produce the supine position. Radiographs are taken and intracavitary irradiation performed with the patient in the supine position.

A shield covering the tissues irradiated from intracavitary sources can then be used when external irradiation is given by two opposing fields in order to obtain an optimum dose. In this way it is considered that the risk of hot or cold spots can be minimized.

Radium treatment combined with external irradiation by anterior and posterior fields is often carried out. In these cases standard shields in the form of central blocks can be used (DiSaia *et al.*, 1975). It has been advocated that the shields should be used primarily in order to protect the bladder and rectum. For this purpose standard shields may be satisfactory. Fletcher (1973) has stressed that it is also exceedingly important to know the exact dose received by the bladder and rectum during radium treatment. As a rule the doses are measured in the bladder and rectum immediately after radium insertion with the patient in the lithotomy position. However, these values are lower when the patient is in the lithotomy position than in the supine position (Joelsson and Bäckström, 1969). This indicates the movements of tissues in the pelvis. Therefore all measurements during radium treatment should be done with the patient in the supine position.

Fletcher (1973) has also stressed the importance of exact calculation of the dose distribution in the pelvis when combined treatment is carried out, in order to obtain the maximum possible cure-rate and to minimize complications. It has been shown that the sources sometimes move during radium treatment (Joelsson, 1970). Therefore it is difficult to discover the exact dose distribution in the pelvis during radium treatment and to achieve accurate shielding.

In order to obtain an exact dosimetry in the central region of the pelvis Chassagne *et al.* (1973) have developed a combined external and intracavitary irradiation technique. They use low dose-rate sources which are fixed in a vaginal mould and the dose distribution in the central part of the pelvis is calculated from radiographs by computer. When external irradiation is given an individualized central shield is constructed using these calculations.

One of the great advantages with the afterloading technique using high intensity sources is that treatment times are very short, normally only a few minutes. The intracavitary catheters are locked in position from outside the pelvis in such a way that they do not move during treatment. An exact dosimetry can be obtained around the sources in the pelvic region. The doses can thus be calculated in different parts of the pelvis when combined irradiation is used. This provides a better possibility to develop the method. Every case developing a complication due to the irradiation can be analysed and the dose to the damaged tissues can be calculated with high accuracy. In addition the dose distribution in the tumour region can be calculated accurately and correlated with local cure.

ACKNOWLEDGMENTS

We would like to thank Mrs. M. Anderson for technical help and Miss A. Rydvall for typing the manuscript.

REFERENCES

ARMITAGE, P., 1973. Comparison of two means, pp. 116–118. Regression pp. 150–156. In *Statistical Methods in Medical Research* (Blackwell Scientific Publication, Oxford).

BECKMAN, K. W., 1971. Computer program for intracavitary dose planning. *Acta Radiologica, Supplementum, 310*, 39–47.

CHASSAGNE, D. J., 1973. Low dose-rate technique of endocavitary brachytherapy. *Proceedings of the Royal Society of Medicine, 66*, 936–938.

DISAIA, P., MORROW, C. P., and TOWNSEND, D. E., 1975. Invasive carcinoma of the cervix. In *Synopsis of Gynaecologic Oncology*, pp. 40–62 (John Wiley & Sons, New York).

FLETCHER, G. H., 1973. Squamous cell carcinomas of the uterine cervix. In *Textbook of Radiotherapy*, pp. 620–665 (Lea and Febiger, Philadelphia).

JOELSSON, I., and BÄCKSTRÖM, A., 1969. Dose rate measurements in bladder and rectum. *Acta Radiologica, 8*, 343–359.

JOELSSON, I., 1970. Radiotherapy of carcinoma of the uterine cervix with special regard to external irradiation. *Acta Radiologica, Supplementum, 302*, 1–99.

JOSLIN, C. A., SMITH, C. W., and MALLIK, A., 1972. The treatment of cervix cancer using high activity ^{60}Co sources. *British Journal of Radiology, 45*, 257–270.

O'CONNELL, D., JOSLIN, C. A., HOWARD, N., RAMSEY, N. W., and LIVERSAGE, W. E., 1967. The treatment of uterine carcinoma using the Cathetron. Part 1. Technique. *British Journal of Radiology, 40*, 882–887.

1979, *British Journal of Radiology*, *52*, 472–477

The treatment of difficult cutaneous basal and squamous cell carcinomata with electrons

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ABSTRACT

The use of electron beam therapy with energies up to 10 MeV in the treatment of basal and squamous cell carcinomata of the skin is described. The results of treatment of 15 cases are presented with photographs of six cases. Excellent clinical and cosmetic results have been obtained. Electron therapy has been found to be simple and convenient, avoiding the necessity for the use of radium moulds in a number of cases and thus avoiding radiation exposure of staff.

Electron therapy for the treatment of malignant lesions has been in use since 1949 (Zuppinger, 1967). In 1970 the use of electron beams with energies up to 10 MeV was reviewed in detail in a paper by Jackson (1970). Since then work has been published on electron therapy in the management of carcinoma of the skin (Tapley, 1975), and in the management of cutaneous manifestations of lymphomata such as mycosis fungoides (D'Angio *et al.* 1975; Fuks and Bagshawe 1971).

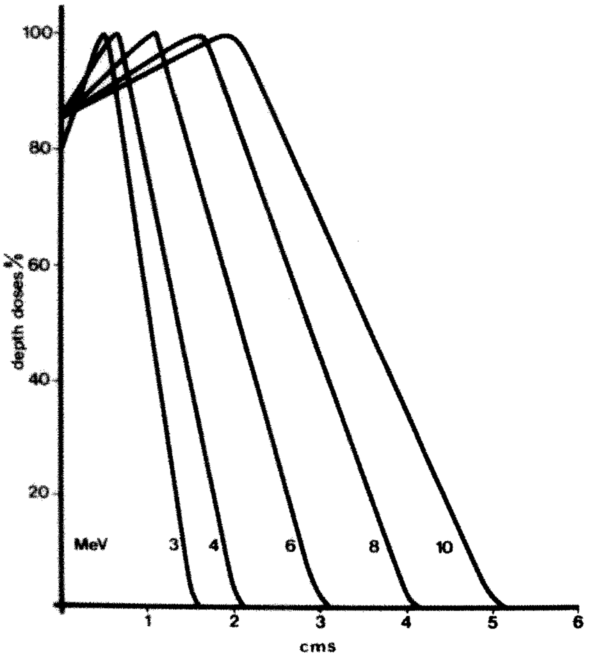


FIG. 1.

Depth-dose curves for electron beams of energies 3, 4, 6, 8, and 10 MeV.

METHOD

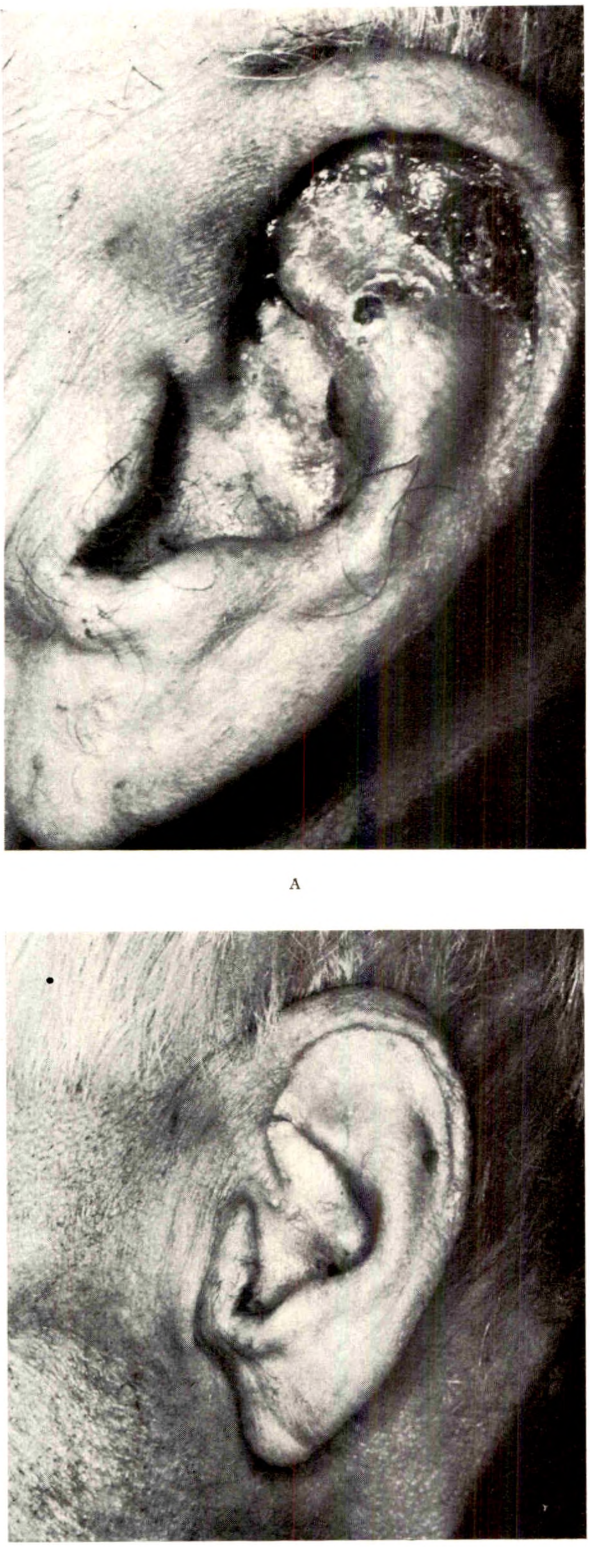
When electron beam therapy is used, it is possible to irradiate superficial lesions with sparing of the deep tissues. This is due to the shape of the depth-dose curve, which shows a fairly flat initial plateau followed by a rapid fall-off in the absorbed dose. There is an initial build-up of dose within the first few millimetres of tissue which produces modest skin sparing. Figure 1 illustrates the depth-dose curves at the energies of electrons available from the SL 75/10 linear accelerator which was installed at Mount Vernon Hospital in 1973. When treating patients with skin tumours, the skin-sparing effect can be overcome by the use of compensating material, usually wet tissue paper. The thickness of wet tissue paper required is 2 mm for 3–4 MeV electrons, 3 mm for 4–8 MeV electrons and 6 mm for 10 MeV electrons. If air gaps need to be eliminated a wax compensator is necessary.

We have only a limited number of applicators available which are circular in shape and of diameter 5, 10, 14 and 17.5 cm. These are modified for irregular shaped fields by the use of lead cut-outs, usually of a thickness of 4–5 mm, which reduce penetration to less than 3%. With 3 and 4 MeV electron beams there is more scatter at the edge of the field and it is therefore necessary to allow a margin of 1 cm around the lesion to ensure adequate dosage.

We decided to treat a selected group of patients in whom it was felt that the megavoltage qualities of electron therapy would be advantageous. These were mainly elderly patients with skin tumours overlying the skull or cartilage, where the possibility of bone or cartilage necrosis was thought to be a risk if low energy photons were used. Two patients had recurrent disease following previous treatment with photons; one refused surgery and the other was thought to be unfit for it. The sites treated included the scalp, pinna, dorsum of the hand and bridge of the nose.

RESULTS AND DISCUSSION

In all we have treated 24 patients but are presenting the results of 15, all of whom have been

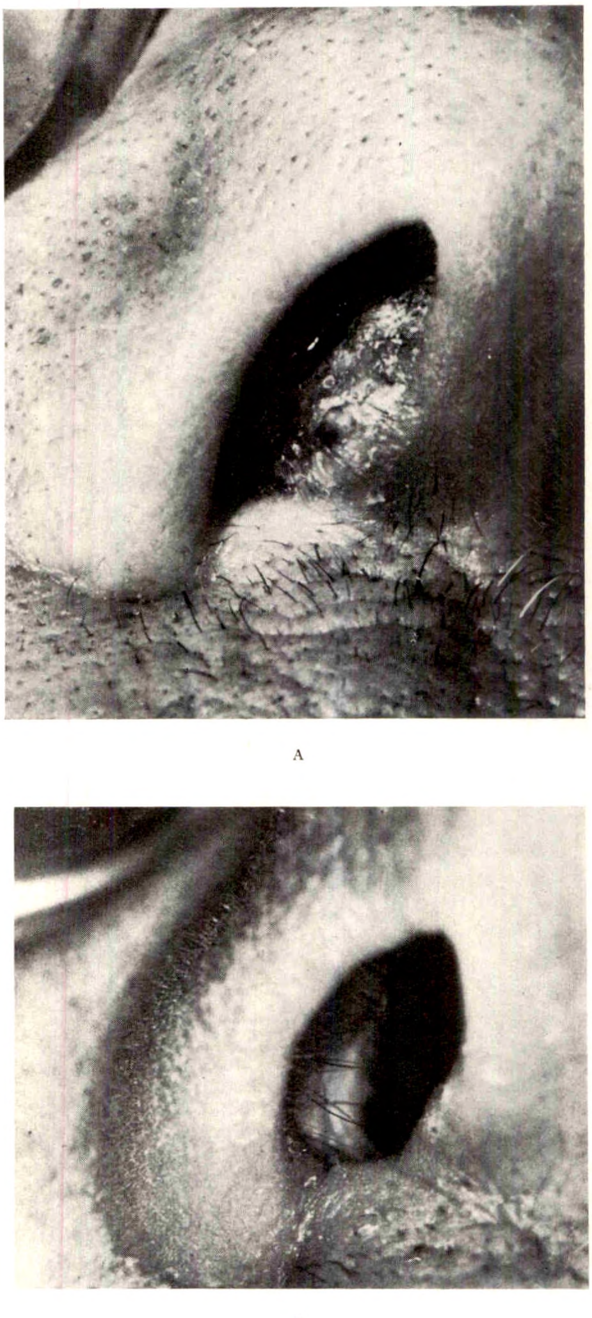


A

B

FIG. 2. *Case 1.*

Comparison of carcinoma before and after treatment. Pinna of ear. (A) Before radiotherapy; (B) After radiotherapy.



A

B

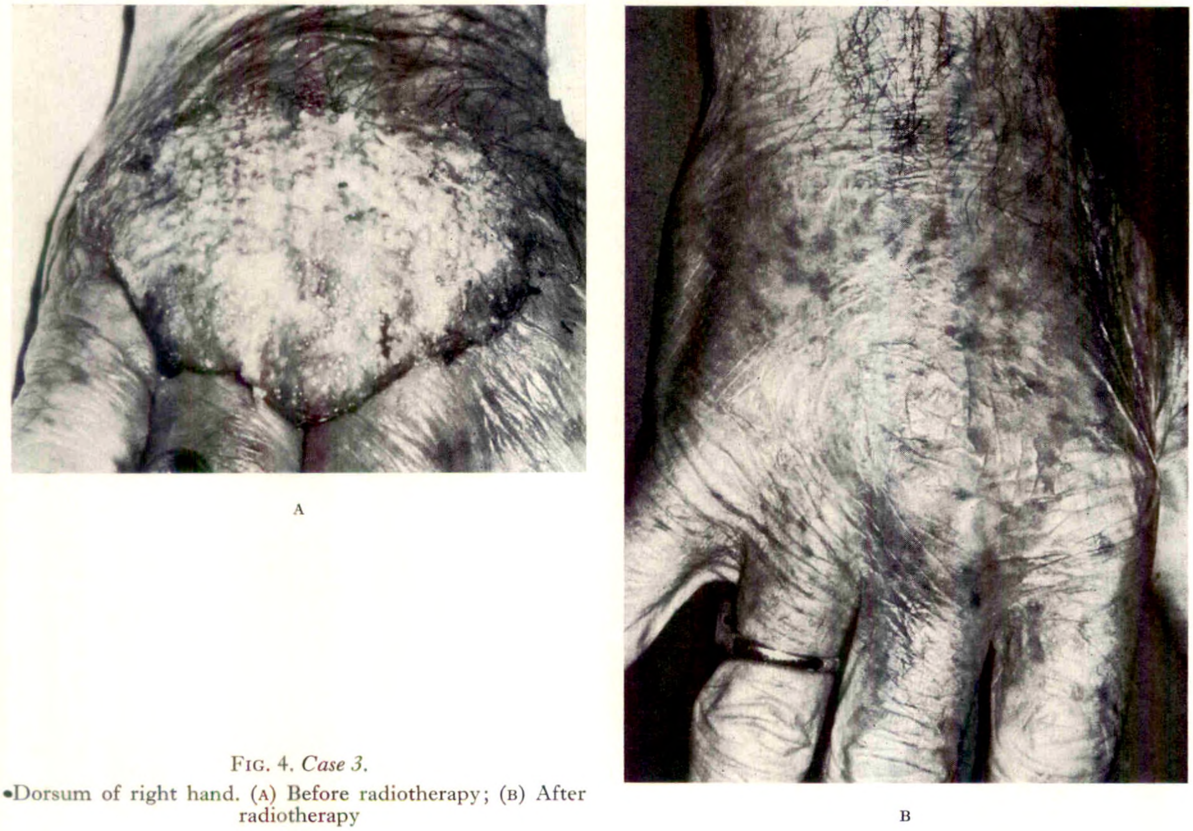
FIG. 3. *Case 2.*

Right nasal vestibule. (A) Before radiotherapy; (B) After radiotherapy.

TABLE I

RESULTS IN PATIENTS ILLUSTRATED IN FIGS. 2–7. BUILD-UP USED WITH ALL PATIENTS

No.	Age	Histology and previous treatment	Site	Treatment	Follow-up
1	83	Basal cell carcinoma	Pinna	5 cm circle 6 MeV 16 fractions in 28 days 4800 rad	15 months No recurrence
2	74	Well differentiated squamous carcinoma	Right nasal vestibule	3 cm circle 10 MeV (wax block) 15 fractions in 19 days 4500 rad	6 months No recurrence
3	78	Well differentiated squamous carcinoma	Dorsum right hand	10 cm circle 10 MeV 15 fractions in 21 days 4500 rad	12 months No recurrence
4	84	Basal cell carcinoma recurrent after soft X rays 4 × 800 rad 1972	Left side nose	5 cm circle 6 MeV 9 fractions in 12 days Dose 4000 rad	6 months No recurrence
5	60	Basal cell carcinoma Incomplete excision 1968, 1972	Anterior neck	10 cm circle 8 MeV 24 fractions in 61 days with gap of 25 days due to skin reaction at 3500 rad; 6000 rad total	6 months 0.7 cm recurrence at edge of treated area. Treated by local excision 18 months No recurrence
6	71	Moderately differentiated squamous cell carcinoma	Scalp	5 cm circle 8 MeV 10 fractions in 14 days 4000 rad	18 months No recurrence


A

B

FIG. 4. *Case 3.*

Dorsum of right hand. (A) Before radiotherapy; (B) After radiotherapy

TABLE II

RESULTS IN NINE OTHER PATIENTS. BUILD-UP USED WITH ALL PATIENTS

No.	Age	Histology and previous treatment	Site	Treatment	Follow-up
7	78	Basal cell carcinoma	Scalp	10 cm circle 6 MeV 20 fractions in 28 days 5000 rad	18 months No recurrence
8	65	Basal cell carcinoma Radiotherapy for ringworm as child	Scalp	6 cm circle 4 MeV 15 fractions in 21 days 5000 rad	9 months No recurrence
9	74	Basal cell carcinoma recurrent after soft X rays; 3 × 900 rad in 5 days, 1971	Bridge of nose	5 cm circle 6 MeV 20 fractions in 28 days 5000 rad	18 months No recurrence
10	70	Basal cell carcinoma recurrent after cautery	Bridge of nose	5 cm circle 6 MeV with Pb mask 10 fractions in 15 days 4000 rad	18 months No recurrence
11	70	Basal cell carcinoma	Dorsum of hand	5 cm circle 8 MeV 10 fractions in 12 days 4000 rad	18 months No recurrence
12	60	Solar keratosis	Dorsum of hand	3.5 cm circle 6 MeV 15 fractions in 21 days 4500 rad	2 years No recurrence
13	69	Squamous carcinoma incompletely excised	Dorsum of hand	10 cm circle 8 MeV 20 fractions in 28 days 6000 rad	2¾ years No recurrence
14	81	Basal cell carcinoma No skull involvement on radiograph	Scalp	10 cm circle 6 MeV 22 fractions in 33 days 5500 rad	Incomplete regression, later regrowth Eventually agreed to have surgery
15	52	Squamous carcinoma Incomplete excision	Left temple	10 cm circle 8 MeV 15 fractions in 21 days 4500 rad	6 months No recurrence Excellent cosmetic result

followed for at least six months. These are presented in detail in Table I (these six patients have accompanying photographs) and Table II. The given doses are similar to those used with photons.

We have been most impressed with the excellent cosmetic and functional results obtained with electron therapy (Figs. 2–7). In general there has been minimal skin reaction, only one case (5) developing moist desquamation which necessitated a break in treatment. So far, recurrent disease has occurred in two cases (5 and 14). In case 5, there was a small recurrence on the edge of the treatment field which was excised successfully. Patient 14 had a very advanced scalp lesion which we now consider was treated with too low an energy and therefore was probably under-treated at depth.

It is not always possible to use surgery for retreatment of recurrent disease following treatment by low energy photons, owing to the general condition of the patient or refusal of surgery. The rapid fall-off in dose at depth with electrons, resulting in the protection of normal tissue, is an advantage of electrons over conventional radiotherapy and we have used electrons in two cases (4 and 9) with recurrent disease. They are both doing well at six and 18 months respectively with no evidence of recurrence or necrosis.

We have treated a number of patients with lesions on the scalp, dorsum of the hand and pinna who, before the advent of electron therapy, we would have treated with a radium mould. We consider that the use of electron therapy in these patients is a considerable advance in that it produces comparable clinical results without the risk of radiation exposure to staff.

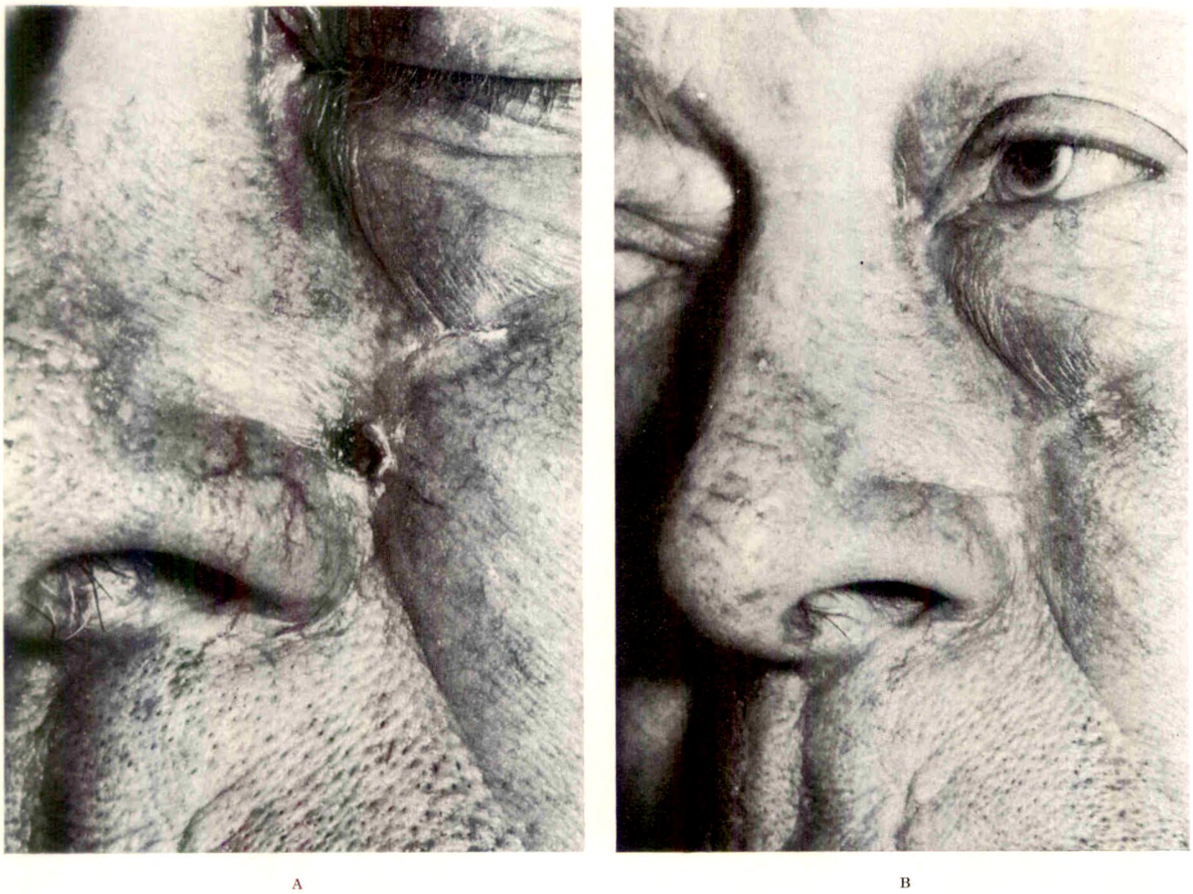


FIG. 5. *Case 4.*
Left side of nose. (A) Before radiotherapy; (B) After radiotherapy.

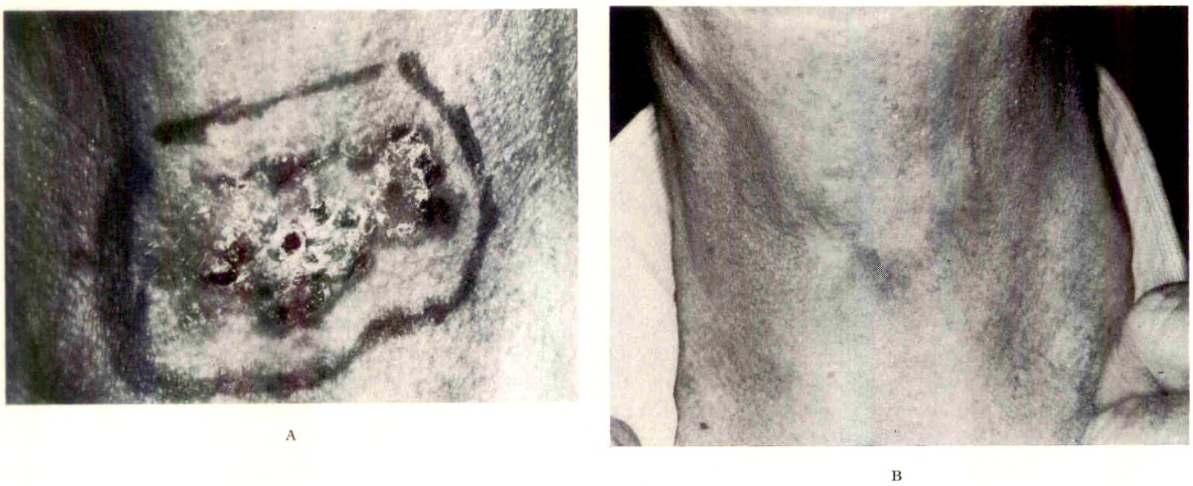


FIG. 6. *Case 5.*
Anterior neck. (A) Before radiotherapy; (B) After radiotherapy.

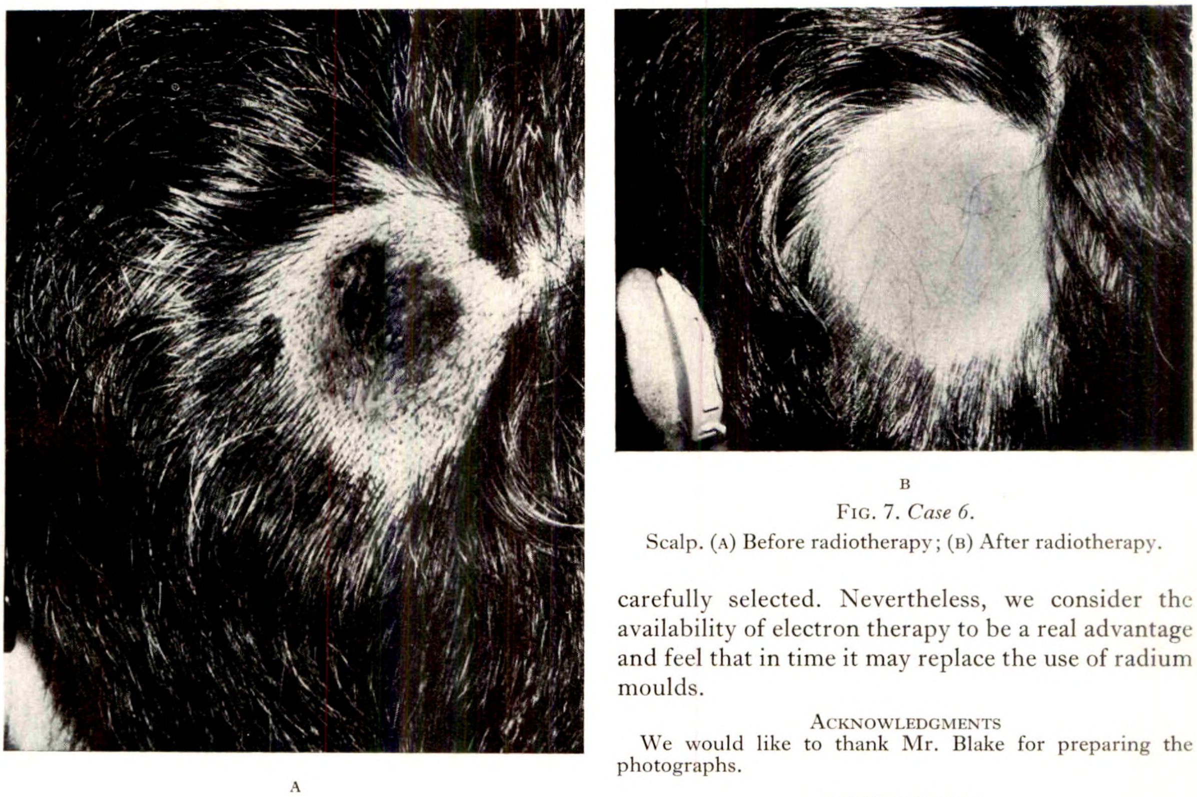


FIG. 7. *Case 6.*
Scalp. (A) Before radiotherapy; (B) After radiotherapy.

It is also possible to avoid the need for complicated treatment plans and set-ups and instead to use a single electron field in difficult sites such as the vestibule of the nose, case 2, and a curved area as in the neck, case 5.

In a busy department, where 800 cases are treated annually on the linear accelerator, the main disadvantage of electron therapy is that it is time consuming. This is mainly because of the necessity to calibrate the machine before each treatment. As a result the patients who are treated have to be very carefully selected. Nevertheless, we consider the availability of electron therapy to be a real advantage and feel that in time it may replace the use of radium moulds.

ACKNOWLEDGMENTS

We would like to thank Mr. Blake for preparing the photographs.

REFERENCES

D'ANGIO, G. J., NISCE, L. Z. and HO KIM, J., 1975. Weekly total skin electron beam therapy for mycosis fungoides and other cutaneous lymphomata; further experience. *British Journal of Cancer*, *31*, Sup. II. 379–385.

FUKS, Z, and BAGSHAWE, M. A., 1971. Total skin electron treatment of mycosis fungoides. *Radiology 100*, 145–150.

JACKSON, S. H., 1970. The clinical application of electron beam therapy with energies up to 10 MeV. *British Journal of Radiology*, *43*, 431–440.

TAPLEY NORAH DU V., 1975. Skin and lips. In *Clinical Applications of the Electron Beam.* Edited by Norah du V. Tapley (John Wiley and Sons. Ashington). 93–123.

ZUPPINGER, A., 1967. Treatment by supervoltage machines–electron beam therapy. In *Modern Trends in Radiotherapy I.* Edited by T. J. Deeley and C. A. P. Wood (Butterworths, London) 250–259.

Book review

A Guide to the X-ray Department. By Myer Goldman, pp. ix+89, illust., 1978 (Bristol, John Wright & Sons Ltd.), £3·00.
ISBN 0–7236–0493–2

The tremendous, rapid advances and changes in radiology are clearly and simply explained in this interesting and easy to read book. It aims to instruct not only nurses, but students of medicine, radiography and pharmacy.

Regrettably, the preparation of patients for special X-ray procedures is only briefly mentioned. We believe good bowel preparation is extremely important if first class films are to be produced—the nurse's responsibility for this preparation could have been given in more detail. Perhaps more emphasis is due on avoidance and awareness of possible reactions to contrast media.

The illustrations and diagrams are good, clear and helpful.

This volume will make a valuable addition to the nurse's bookshelf and to the ward library.

R. J. FRANCE,
C. E. CLARKE.

1979, *British Journal of Radiology*, *52*, 478–481

A computerized three-dimensional treatment planning system utilizing interactive colour graphics

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ABSTRACT

A new computerized radiation treatment planning system has been developed to aid in three-dimensional treatment planning. Using interactive colour graphics in conjunction with a PDP 11/45 computer, the system can take multiple transverse contours and construct a perspective display of the treatment region showing organ surfaces as well as cross-sectional contours. With interactively selected orientations, the display allows easy perception of the relative positioning of the treatment volume and neighbouring anatomy. For external beam treatment planning, interactive computer simulation is used to select diaphragm sizes which best conform to the target area while avoiding sensitive structures.

Dose calculations for the selected beams are carried out on multiple transverse planes. The calculational planes and surfaces are displayed in perspective with radiation dosage displayed in an interactively manipulated colour display. Altogether the system provides an easy assessment of the volume to be irradiated, interactive selection of optimal arrangements of treatment fields and a means for visualizing and evaluating the resulting dose distributions.

Following earlier work in the Department of Radiation Oncology at Rhode Island Hospital in development of a three-dimensional radiation treatment planning system, a new interactive computerized planning system has been developed. The new system uses colour graphics to provide better insight into the planning of radiation treatments which will best conform the radiation distribution to the target volume while minimizing radiation elsewhere, especially to sensitive organs. The new system is designed to help the planner visualize relative anatomy within the proposed treatment volume, simulate proposed treatment fields relative to this anatomy, and make qualitive and quantitative assessment of dose throughout the treatment volume.

The earlier work at the Rhode Island Hospital approached the problem of three-dimensional planning of external beam treatments by using reconstructed multi-plane images taken from transverse axial tomographs (Reinstein *et al.*, 1978). In that approach, contours at multiple levels could be viewed in three-dimensional perspective and rotated. The main advantage of this method was that contours could be placed in orientations which would simulate their position relative to an incoming beam. Using this method, gantry angles, collimator angles, beam width, and height and blocking could be determined. A disadvantage was that the system was not entirely interactive and required a number of time-consuming trial and error tests. Further, the resulting dose distribution could only be represented by using conventional two-dimensional isodose displays.

The system reported here removes many of these disadvantages. Using colour video image hardware and computer generated graphics, transverse contours and reconstructed surfaces are displayed in three-dimensional perspective with colour used to differentiate anatomical features. Interactive graphics have been developed to enable the treatment planner to simulate beams for external treatment planning. Further, the radiation dosage can be calculated for multiple planes and surfaces and can be displayed using a colour representation of the dose distribution.

METHODS AND EQUIPMENT

The new display software is implemented on a Digital Equipment PDP 11/45 mini-computer with floating point hardware and 80k words of core memory. The computer operates with a multi-partitioning time-sharing operating system that supports up to twelve terminals. The colour image display hardware is made by DeAnza Systems, Inc. and was purchased with interfacing to the PDP 11 system.

The graphics software uses an interactive console which contains four push buttons, four potentiometers and a "joy-stick" with two additional potentiometers. The graphics software is written to use the interactive console exclusively with no terminal input. Cues for the colour-coded buttons and potentiometers are displayed in annotation fields so that the buttons and knobs are easily programmed for different functions. A schematic for the computer system is shown in Fig. 1.

The program is written primarily in Fortran and currently consists of nine overlays each running in

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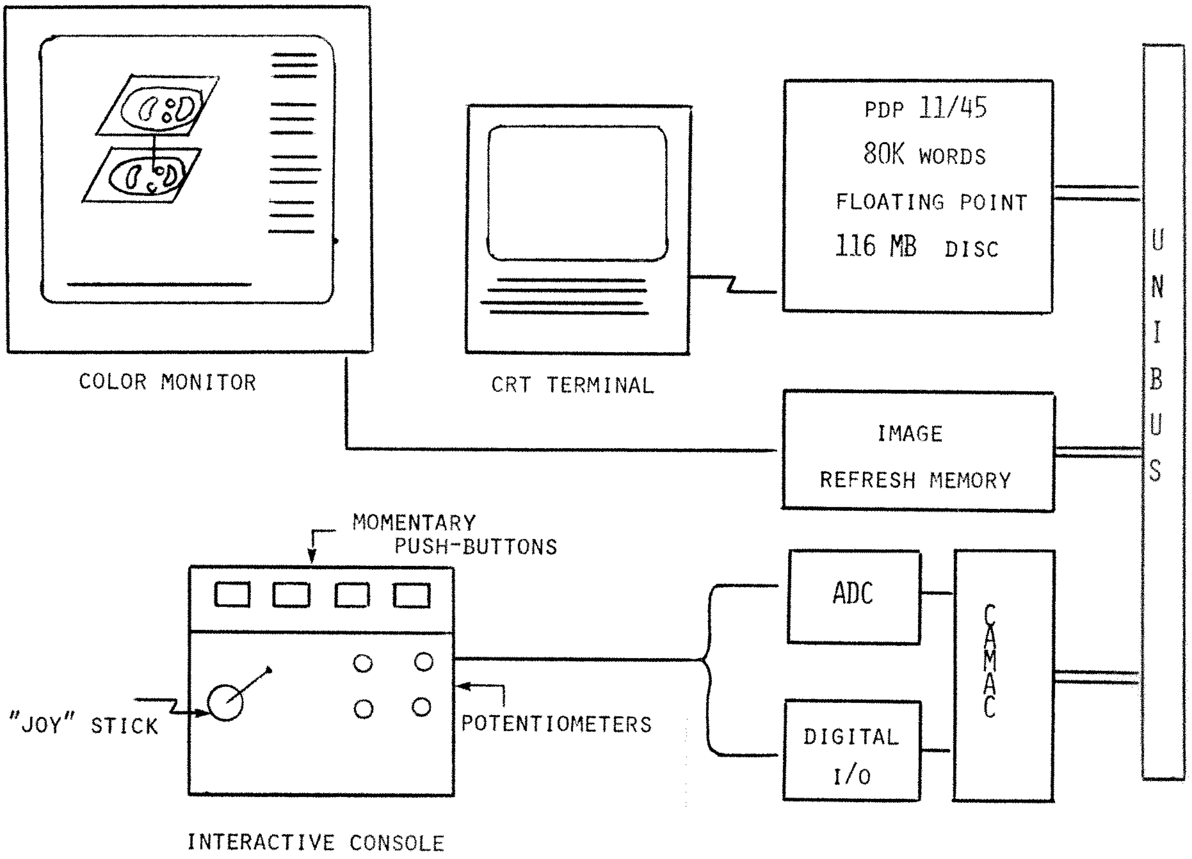

FIG. 1.
Schematic of computer and graphics system.

less than 16k of core. The software is interfaced with the conventional treatment planning programs and can be entered from the external beam planning program.

As described in the earlier paper, a separate program in the conventional planning system is used to enter contour data with a sonic-digitizer from transverse axial tomography films. Individual contours are labelled by organ type and the relative positioning of the transverse level. For a typical case, about five levels are required throughout the proposed treatment area. Once entered, these contours are available for three-dimensional reconstruction.

Anatomical display

Figure 2 shows a perspective reconstruction of three of five transverse planes taken in the region between the thoracic inlet and the mid-line thorax region. The planes were taken at a relative spacing of +7, +3, 0, −4, and −7 cm. The planes at +3 and −4 cm are not shown in Fig. 2 but were used for the surface reconstruction. The contours in Fig. 2 are distinguished by colour with the external contour in blue, the lungs in white, the spinal cord in green, and the target (in this case the oesophagus) in yellow. The front surfaces of the spinal cord and target are shown as well as the back surface of the right lung. This figure graphically illustrates the variation of the relative anatomy throughout the volume to be irradiated.

For the perspective displays the orientations and magnifications are selected interactively through the use of the console potentiometers. The image can be expanded along any of the original axes (used in Fig. 2 to increase separation between planes). Contour line elements are removed when hidden by any of the planes (rectangular limits used).

The surfaces are constructed using the outline data on all of the transverse levels taken. The reconstruction begins by defining a set of mesh points which are uniformly spaced around each outline. Spacing for the points is determined by calculating the total chord or path length and dividing this length by the number of desired segments (30 for this example). The points are aligned on each level by first calculating a mean or average centre. A line is then drawn through the centre parallel to one of the co-ordinate axes. The most positive intercept of this line with the outline is taken as a starting point for generating the mesh. For interpolation between transverse levels, the generated mesh points are connected to their aligned counterparts with a smooth curve, constructed by using spline curve-drawing techniques (Ahlberg, 1974). The technique takes the initial set of co-ordinate points and derives a larger set of mesh point values separately for each of the three dimensions. The interpolated values are constrained to a curve which passes through the initial set of values and which exhibits no discontinuities in its slope. For Fig. 2, a set of 20 mesh points has been generated for each set of points around the outlines. The result of these two interpolation operations is a grid of three-dimensional co-ordinates which map out the surface.

All of the contour surface maps are generated and stored prior to entry into the three-dimensional display system. Within the display system, individual surfaces may be recalled and displayed showing either their front or back (away from viewer) surfaces.

Radiation beam selection

After a look at the relative anatomy within the proposed treatment region, treatment planning for external beam therapy may proceed by selecting one of two beam simulation modes. The first mode is similar to conventional planning systems which allow interactive selection of beam parameters. It differs in that beam paths along the transverse planes can be displayed simultaneously and manipulated on the multi-plane perspective images. The second mode of simulation is particularly suited for aligning

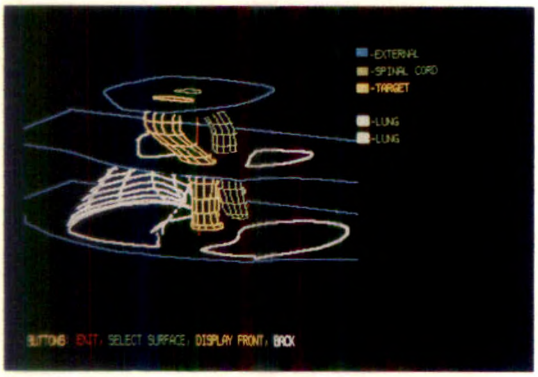

Figure 2: Multiple cross-sectional contours and organ surfaces in three-dimensional perspective.

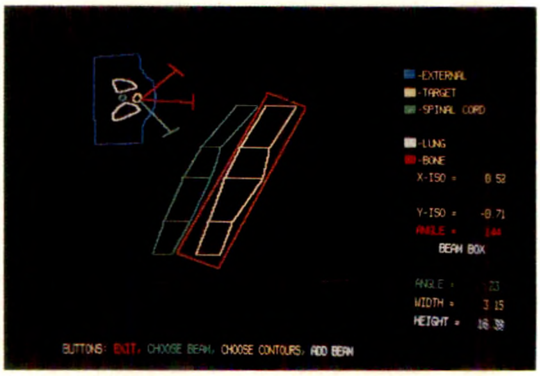

Figure 3: Simulation of external beams. The red rectangle shows the beam area enclosing the target but avoiding the spinal cord.

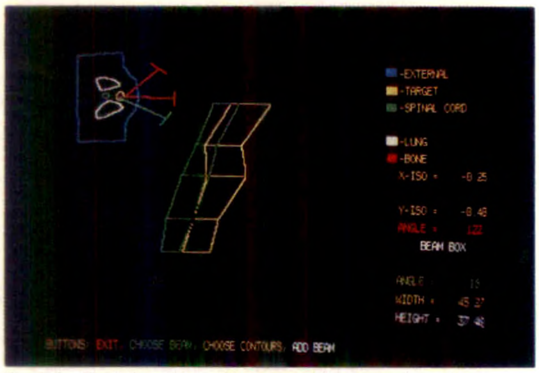

Figure 4: Simulation of beam with unnacceptable overlap of target and spinal cord. At this orientation part of the spinal cord is inevitably included in the field.

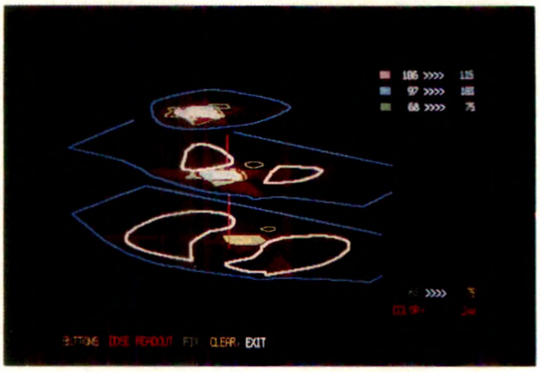

Figure 5: Coloured dose distribution on perspective multiplanar display.

individual beams. A typical display for this mode is shown in Fig. 3. In this figure, the contours for a single transverse plane are shown in the upper left hand corner along with the relative beam positioning. In the centre of the display is shown the simulation of a field area (shown in red) whose central axis is parallel to the transverse planes. The projection of the spinal cord (in green) and the target (in yellow) are shown relative to the incoming beam, the incident direction of which can be seen by the positioning of the green beam shown in the upper left hand corner. This direction may be interactively rotated by adjusting a potentiometer. The treatment field shown in Fig. 3 is one of two proposed lateral exposures which are planned to avoid irradiation of the spinal cord while minimizing exposure of the lung. At a fully lateral angle, the lung would receive too much dose, therefore the beam is moved anteriorly. If the beam is moved too far forward, the target area and the spinal cord overlap. A simulation of an unacceptable overlap can be seen in Fig. 4. Figure 3, on the other hand, shows adequate separation. Besides altering the incident direction of the beam, the width, height, tilt (collimator angle) and centre may be interactively adjusted relative to the anatomy so as best to conform the radiation area to the target area.

Three-dimensional isodose display

To evaluate the proposed treatment plan, it is, of course, necessary to calculate and display the resulting dose distribution at points within the target as well as at neighbouring locations. For three-dimensional planning, this implies calculations throughout the irradiated volume. While the new system is capable of displaying dose distributions on nonparallel planes and surfaces, at present the dose calculations for external beam therapy are limited to planes which are coplanar or parallel to the central axes of the beam combination. Normally, calculations are carried out on the planes used for input of contour. The calculations are currently the slowest part of the three-dimensional planning system and require about two minutes per plane. The calculational program used is a version of J. R. Cunningham's CBEAM program (Gupta and Cunningham, 1966). The calculation divides the dose into two components–primary and scattered radiation. The primary contribution is obtained by using tissue-air ratios for zero area and by making appropriate geometrical corrections to account for inverse-square fall-off, compensating filters, and penumbra effects. The scatter component is calculated by integration of differential scatter-air ratios which are generated using a table of scatter–air ratios. The dose is calculated at a matrix of points across the plane and the data are stored in a magnetic disc file for later display and evaluation.

Instead of displaying conventional isodose lines, the relative dose is evaluated and loaded into each display pixel that projects onto a calculational plane. This process takes only a few seconds. Using intensity transformation hardware on the display system any colour can be assigned to any dose level. For evaluating the dose, the potentiometers on the console are used to set and vary the lower limit and width of one or more bands of uniform colour. These bands reflect in radiated areas which lie between two dose limits. Because the colour-to-dose assignment is easily made, the limit adjustments are highly interactive and simultaneous for the entire display area. Used in combination with the perspective display, the user gains an immediate perception of the dose distribution throughout the irradiated region.

Figure 5 shows a perspective display of the planes with dose calculations added. A background of red whose intensity is proportional to the dose shows the radiation paths. Three bands of colour have been selected for this display. Each band shows a uniformity of dose across the target area for each of the three levels. However, the percentage difference between bands shows a problem of uniformity of dose along the length of the tumour (corrected in practice by a wedge compensator).

While the examples shown here relate to the thorax region, the same techniques of three-dimensional display can be applied to other sites in the body. Particularly in the pelvis, the uterus, bladder and rectum can be displayed relative to the external contour and bony pelvis. Isodose calculations for intracavitary sources can be shown in the same manner as for an external beam and can be combined with external beam calculations to show the composite doses in relation to the pelvic anatomy. The use of this system for the pelvic region will be published shortly.

REFERENCES

Ahlberg, J. H., 1974. A picture-view of splines. Technical Report Brown University, Providence, Rhode Island.

Gupta, S. K., and Cunningham, J. R., 1966. Measurement of tissue–air ratios and scatter functions for large field sizes for cobalt 60 gamma radiation. *British Journal of Radiology*, *39*, 7–11.

Reinstein L. R. McShan D. L. Webber B. M., and Glicksman A. S. 1978. A computer-assisted three-dimensional treatment planning system. *Radiology*, *127*, 259–264.

1979, *British Journal of Radiology*, *52*, 482–484

The dose in water surrounding point isotropic gamma-ray emitters

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ABSTRACT

A Monte Carlo method has been used to calculate the dose distribution around point γ-ray emitters in water. Five γ-ray emitting radionuclides, ^{60}Co, ^{137}Cs, ^{192}Ir, ^{198}Au and ^{226}Ra, which are commonly used in radiotherapy interstitial implants, have been considered. The results are in substantial agreement with those derived using a combination of experimental and theoretical data.

The distribution of dose around an interstitial implant depends both on the geometry of the implant and the energy spectrum of the implanted radionuclide. Most dosimetry schemes comprise discrete summations of point distributions taken over the geometry of the implant. The fundamental data concerning the distribution of dose in water around a point isotropic γ emitter are, however, uncertain. Meisberger *et al.* (1968) have shown that the experimentally determined ratio of exposure in water to exposure in air as a function of distance from a point source disagrees with theoretical results based on the energy absorption build-up factors of Berger (1968). The experimental data of several authors are cited but none are in agreement with the calculated distribution. For gold 198 and iridium 192 this discrepancy is of the order 5% at 10 cm distance and is somewhat less for caesium 137, cobalt 60 and radium 226. Meisberger *et al.*, in the absence of any corroborating evidence, recommend for clinical use a third order polynomial fit to the average of theoretical and experimental results. The polynomial fit for ^{192}Ir has been in use in this hospital for some years (Dance—private communication). It is the purpose of this paper to present results from Monte Carlo calculations which lend support to the recommended curves.

THE MONTE CARLO MODEL

The philosophy of the Monte Carlo model is that the bulk properties of the photon-tissue interaction can be simulated as the ensemble of constituent single photon behaviour. A computer program has been constructed to trace the passage of photons from a point isotropic emitter through a uniform medium. The model is an analogue Monte Carlo simulation in that no attempt has been made to force interactions (Raeside, 1976). The details of computing both the location of interaction sites and the subsequent nature of the interaction have been described in an earlier paper on the interaction of external beam X radiation with inhomogeneous media (Webb and Parker, 1978). The relative probabilities for Compton interaction, photoelectric interaction and pair production have been determined by linear interpolation of the energy dependent cross sections in the region 10 keV $\leqslant E \leqslant$ 10 MeV utilizing the data for water of White-Grodstein (1957). These data for Compton interactions differ

TABLE I

COMPUTED PARAMETERS WHICH CHARACTERIZE THE PHOTON INTERACTIONS

	^{192}Ir	^{198}Au	^{137}Cs	^{60}Co	^{226}Ra
Fraction of first collisions which are photoelectric interactions	0.002	0.001	0.026	0.000	0.006
Fraction of first collisions which are Compton interactions	0.936	0.928	0.867	0.797	0.871
Fraction of first collisions which are pair-production interactions	0.000	0.000	0.000	0.000	0.001
Fraction of first collisions which take place beyond $r = 0.25$ m	0.062	0.071	0.106	0.203	0.122
Average number of collisions per photon	6.76	6.59	5.54	4.57	5.58
Fraction of energy given to photoelectrons	0.044	0.035	0.020	0.006	0.017
Fraction of energy given to Compton electrons	0.602	0.608	0.605	0.567	0.556
Fraction of energy given to pair products	0.000	0.000	0.000	0.000	0.000
Fraction of energy leaving the water phantom	0.355	0.357	0.375	0.427	0.425
Total computing time (sec)	1040	1003	870	706	879

by less than 1 % from the more recent compilation of Hubbell (1969). Although the difference is more marked for photoelectric interaction, reference to Table I shows that the major contribution to dose arises from Compton scattering. The cross sectional data yield the energy dependent linear attenuation coefficient needed to determine the distance to an interaction site. For a detailed discussion of the assumptions made concerning electron production and energy deposition we refer readers to the paper by Webb and Parker (1978), where it is shown that the finite range of Compton and photoelectrons has been carefully modelled.

The initial photon energy for each history has been selected according to the decay scheme of the radionuclide (Martin and Blichert-Toft 1970; Dillman and Von der Lage 1975). Photons are emitted isotropically and we have utilized spherical symmetry to improve the convergence of the Monte Carlo model. Instead of monitoring the electron energy deposition along one specific radius vector, which would make use of only a fraction of the information generated by the photon histories, we have transferred to co-ordinate *r* all energy deposited in the annulus of radius *r*. In this way each photon trajectory contributes information to the dose distribution.

It is emphasized that this model immediately yields the radial distribution of dose rather than exposure. It differs from the calculations cited by Meisberger *et al.* (1968) in that it does not rely on tables of energy absorption build-up factors and makes no assumptions concerning scattered radiation. In this sense, the Monte Carlo model is more fundamental in that absorption and scatter arise naturally from scattering cross sections.

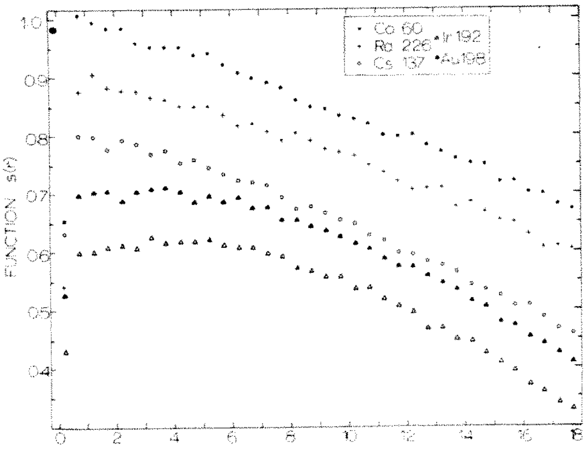

Fig. 1.

Radial dependence $s(r)$ of the dose-rate in water normalized to unity at 1 cm with inverse square law dependence removed. The scale applies directly to ^{60}Co (●). Each point on successive graphs has been displaced linearly by the following amounts: by -0.1 units (+), by -0.2 (○), by -0.3 units (▲), by -0.4 units (△).

Results and Discussion

The radial dependence of the dose-rate in water is shown normalized to unity at 1 cm in Fig. 1 for the radionuclides ^{60}Co, ^{137}Cs, ^{192}Ir, ^{198}Au and ^{226}Ra (in equilibrium with daughter products); $s(r)$ represents the radial dependence of the absorbed dose-rate in water with the inverse square law fall-off removed to emphasize the effects of scatter and absorption which account for the features of the curves. The computer calculations have been performed for a point isotropic emitter at the centre of a sphere of radius 25 cm. It has been shown by Ellett (1969) that the dose at any distance r is the same in any spherical absorber provided the boundary R of that absorber is at least one photon mean free path λ from the point of interest, *i.e.* $(R-r)\gtrsim\lambda$. For this reason we believe the curves shown in Fig. 1 exhibit no boundary effects. The dose rate $d(r)$ at radius r can easily be found from the plotted curve $s(r)$ by using the inverse square law together with the constant D, the absorbed dose rate in water per becquerel at 1 m,

that is, $$d(r)=\frac{Ds(r)}{r^2} \quad \text{Gy } s^{-1}\text{ Bq}^{-1} \quad . \quad . \quad . (1)$$

The constant D for each radionuclide is listed in Table II. The information in Fig. 1 has been obtained by monitoring 700 000 photon histories. The computer requirements vary according to the radionuclide but are of the order of 1000 sec on a CDC 7600 machine. A parameter of some interest when comparing computer studies on different machines is the number of histories per second. Our

TABLE II

Radionuclide constants D and Γ

Radionuclide	D (Gy m^{2}s^{-1}Bq^{-1})	Γ (C kg^{-1}m^{2}s^{-1}Bq^{-1})
^{192}Ir	3.20×10^{-17}	8.86×10^{-19}
^{198}Au	1.64×10^{-17}	4.50×10^{-19}
^{137}Cs	2.35×10^{-17}	6.41×10^{-19}
^{60}Co	9.52×10^{-17}	2.50×10^{-18}
^{226}Ra	*6.47×10^{-17}	†1.60×10^{-18}

The more familiar units of rad cm^{2}hr^{-1}mCi^{-1} and R cm^{2}hr^{-1}mCi^{-1} may be obtained by multiplying the numbers given by 1.33×10^{17} and 5.16×10^{18} respectively.
*Unshielded and in equilibrium with daughter products.
†Shielded by 0.5 mm Pt and measured experimentally.

figure of 700 histories per second is for example twelve times faster than the corresponding study by Ellett *et al.* (1968) of the dose distribution around monoenergetic point emitters performed on an IBM 7094 machine.

We have, for comparison purposes, also tabulated the specific γ ray constant Γ evaluated from the expression (Trott—private communication),

$$\Gamma = 2.34 \times 10^{-3} \Sigma_i (\mu_{en})_i \Delta_i \quad C\,\mathrm{kg}^{-1}\,\mathrm{m}^2\,\mathrm{s}^{-1}\,\mathrm{Bq}^{-1} \quad . \quad . \quad . \quad . (2)$$

where $(\mu_{en})_i$ ($\mathrm{m}^2\mathrm{kg}^{-1}$) is the energy absorption coefficient for species of energy E_i whose equilibrium dose constant is Δ_i (kg Gy $\mathrm{Bq}^{-1}\,\mathrm{s}^{-1}$). Data for $(\mu_{en})_i$ has been interpolated from NBS Handbook 78 (1961) and Δ_i from Dillman and Von der Lage (1975). An ionization constant of $w = 34$ ev/ion pair has been used. The comparison is not strictly valid because in formulating Γ no account is taken of secondary scatter or of build-up. An approximate numerical equivalence can be obtained by using a "$C\,\mathrm{kg}^{-1}$ to gray factor" of 37.4, valid in the region from 200 keV to 2 MeV. It would not be expected that D would numerically equal Γ. It should be emphasized, however, that for clinical dose measurements equation (1) is simpler to use and more relevant than an expression based on the use of equation (2).

If the data in Fig. 4 of Meisberger *et al.*, can be interpreted as representing the radial fall off in dose rate with the inverse square law removed, our results are seen to differ from both calculated and experimental data, falling almost exactly on Meisberger's "selected average". It should be pointed out that we have modelled only photon interactions and have assumed that electrons have been filtered at source. The material providing this filtration may lead to a build-up close to the origin which we have not superimposed on our distributions.

In calculating the dose-rate around specific radionuclide point sources we have extended similar calculations for monoenergetic point sources by Ellett *et al.* (1968) and Ellett (1969). It is possible to compare their analysis with the present one by estimating the dose-rate at 1 cm for a ^{137}Cs source using their table of point specific absorbed fraction which includes data at 662 keV and 30 keV. This yields a value of 2.47×10^{-17} Gy $\mathrm{m}^2\,\mathrm{s}^{-1}\,\mathrm{Bq}^{-1}$ which is in disagreement with the value of D in Table I by about 5%. Additionally their data predict that the radial fraction $s(r)$ at $r = 10$ cm for ^{137}Cs is 0.89 which differs by 4% both from our result and from the experimental data of Meisberger *et al.* (1968).

Conclusion

The distributions of dose around five point isotropic γ-ray emitters in frequent use have been calculated from first principles by Monte Carlo methods. The distributions differ slightly from previous calculations and experimental data. Whilst such discrepancies are probably unimportant clinically for single point implants (being heavily masked by the inverse square law), they may be significant when collections of point distributions are integrated to yield the total dose from an extended source distribution.

Acknowledgment

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REFERENCES

Berger, M. J., 1968. *Energy deposition in water by photons from point isotropic sources* (MIRD Pamphlet No. 2, National Bureau of Standards, Washington D.C.).

Dillman, L. T. and von der Lage, F. C., 1975. *Radionuclide decay schemes and nuclear parameters for use in radiation-dose estimation*, NM/MIRD Pamphlet No. 10.

Ellett, W. H., Brownell, G. L., Reddy, A. R., 1968. An assessment of Monte Carlo calculations to determine γ-ray dose from internal emitters. *Physics in Medicine and Biology*, *13*, 219–230.

Ellett, W. H., 1969. Specific absorbed fractions for photon point sources within a scattering medium. *Physics in Medicine and Biology*, *14*, 615–625.

Hubbell, J. H., 1969. *Photon cross sections, attenuation coefficients and energy absorption coefficients from 10 keV to 100 GeV*, National Bureau of Standards (U.S.) NSRDS-NBS 29.

Martin, M. J. and Blichert-Toft, P. H., 1970. *Radioactive atoms auger—electron, α—, β—, γ— and X ray data*, Nuclear Data Tables, Vol. 8, Nos. 1–2.

Meisberger, L. L., Keller, R. J., and Shalek, R. J., 1968. The effective attenuation in water of the γ rays of gold 198, iridium 192, caesium 137, radium 226 and cobalt 60. *Radiology*, *90*, 953–957.

NBS Handbook 78, 1961. Report of the International Commission on Radiological Units and Measurements (ICRU).

Raeside, D. E., 1976. Monte Carlo principles and applications. *Physics in Medicine and Biology*, *21*, 181–197.

Webb, S., and Parker, R. P., 1978. A Monte Carlo study of the interaction of external beam X radiation with inhomogeneous media. *Physics in Medicine and Biology*, *23*, 1043–1059.

White-Grodstein, G., 1957. *X-ray attenuation coefficients from 10 keV to 100 MeV*, NBS circular-583.

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Lack of correlation between villus and crypt damage in irradiated mouse intestine

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ABSTRACT

It has been observed that scanning electron microscopy is a more sensitive indicator of mucosal damage at low radiation dose levels than conventional quantitative crypt counting techniques. Three different fractionation schedules were subjected to investigation by both of these methods to try and elucidate some features of irradiation damage to the whole of the intestinal mucosa, at dose levels commonly used in clinical practice. Despite variations in the qualitative observations, there was a marked difference in two of the schedules between damage expressed as crypt counts and that described by the qualitative techniques. In the first case high crypt numbers were associated with severe mucosal damage, whereas the second schedule produced a reduced crypt count in association with low damage to the surface mucosa.

A third schedule produced results in which there was a general agreement between low crypt numbers and considerable surface mucosal damage. However, observations were made of mucosal formations not previously seen on damaged mucosal surfaces. These resembled the appearance normally associated with the gut of patients suffering from coeliac disease. Variations in the qualitative observations were seen in all the schedules so that their interpretation in terms of perturbation of cellular kinetics is difficult.

One of the most important normal tissues which limits the dosage of radiotherapy is the gastrointestinal tract. It is for this reason that a considerable amount of data are available describing both the kinetics and the radiobiological response of gut. Following the development of the microcolony assay of intestinal crypt survival (Withers and Elkind, 1970), Withers and his colleagues have made a detailed study of the response of mouse jejunum to fractionated radiotherapy (Withers *et al.*, 1976) and other workers have complemented this with analyses of the cell population in the crypts (Hendry and Potten, 1974). By contrast there remains a dearth of information about the response of the intestinal villi to radiation. Since the villi represent the functional "compartment" of the intestinal mucosa it is important to investigate the extent to which the radiobiological response of the stem cell compartment in the crypts can be correlated with that of the villi to which such cells migrate.

In a previous paper (Hamlet *et al.*, 1976) we described an examination of the surface appearance of jejunal villi using scanning electron microscopy of aliquots of mouse gut which had also been examined by the microcolony assay technique following irradiation with γ rays or fast neutrons. We observed differences between the effects on the surface morphology of these two forms of radiation at points of radiobiological equivalence in terms of crypt counting. We also found detectable changes in the surface morphology of the villi after dosage levels well below the limit of resolution by the crypt counting technique.

We have now investigated the consequence, in terms of damage to the villus surface, of three régimes of fractionated radiotherapy chosen to mimic those which may be used in clinical practice. The scanning electron microscopical appearances have been analysed using a semi-quantitative approach and these results have again been compared with quantitative data from the orthodox crypt-counting assay technique applied to aliquots of jejunum from the same mice.

MATERIALS AND METHODS

Adult male and female C_3H/He mahogany mice (from Bantin & Kingman Ltd., Hull) 10 to 15 weeks old were irradiated using the fractionation schedules described below. Assay was made $3\frac{1}{2}$ days after the final irradiation dose was administered to allow crypt regeneration to a size sufficient for accurate assessment. The mice were killed and tissues prepared for light and electron microscopy. All histological and microscopy techniques used were as previously described (Hamlet *et al.*, 1976). A minimum of eight mice per treatment were used in all the schedules. The time of irradiation within schedules was kept constant to avoid any artifacts due to circadian rhythms. Postmortem examination was made of animals dying before the day of assay.

Irradiation procedures and dosimetry

The whole-body exposures were made with cobalt 60 γ rays and were carried out on an Orbitron therapy unit. A Perspex jig containing four animals was positioned in its broadest field such that the centre line of each mouse was 40 cm from the source; the dose rates to the tissue under these conditions, approximately 180 rad min^{-1} over the period of the experiments, were measured using a tissue-equivalent chamber which was placed at the centre of a Perspex mouse phantom in the jig. This chamber was in turn calibrated against an NPL secondary standard Farmer-Baldwin ionization chamber under standard conditions.

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The partial body exposures were carried out using a Siemens Stabilipan I unit operating at 250 kV and a current of 15 mA. Beam filtration gave an HVL of 1.85±0.05 mm Cu.

Mice were restrained in Perspex tubes which were positioned so that the abdominal cavity was over a 2.5 cm wide slot cut in a 3 mm thick lead sheet. Measurements of dose rate were made in a Perspex phantom with an ionization chamber both over the centre of the slot and 1.5 cm from its edge, where the femur was judged to be. The femoral dose was less than 4% of the intestinal dose. The suitability of this phantom was checked by comparing this dose rate to measurements made with an ionization chamber placed in the abdominal cavity of a dead mouse. The difference was less than 3%. The profile of dose across the slot was determined using LiF thermoluminescent dosemeters. LiF rods were inserted at 0.5 cm intervals in a Perspex block which was positioned over the slot and irradiated. As a check on the relative doses at the intestines and femora, LiF rods were inserted at these sites into a dead mouse and irradiated. All measurements of dose rate were made using a calibrated Farmer-Baldwin dosemeter. The dose rate obtained was 75 rad min^{-1}.

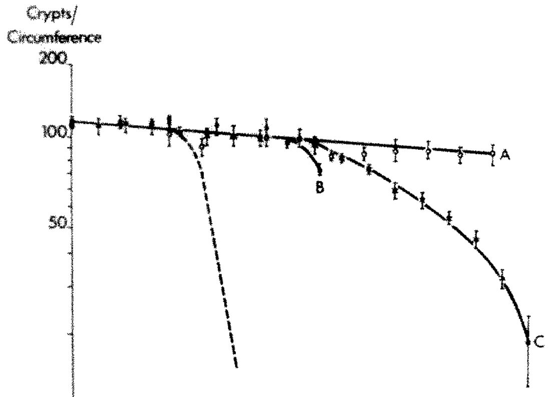

Fig. 1.

Crypt survival curves for Schedules A, B, and C and single dose ^{60}Co gamma irradiation (dotted line).

The Irradiation schedules

Schedule A (whole body)

300 rad daily fractions of ^{60}Co gamma rays plus "assay" dose

Mice were irradiated with 300 rad daily to a total of ten fractions. There was a two-day gap between the fifth and sixth fractions. Twenty-four hours after the final 300 rad dose an "assay" dose of 900 rad was administered to try and reduce crypt cellularity and hence total crypt number.

Schedule B (whole body)

450 rad daily fractions of ^{60}Co gamma rays

Mice received daily fractions of 450 rad to a total of five fractions in five days.

Schedule C (partial body)

250 rad fractions of X rays administered three times per day

Mice received three fractions of 250 rad daily to a total of 18 fractions in six days. The three fractions were given during the day with three hours between fractions and hence the mice had an 18 hour period overnight when no irradiation was administered.

RESULTS

Regenerating crypts

Figure 1 shows dose-response data for the effect on crypt regeneration of the three fractionation schedules. The curves were fitted by eye and, because there was no significant difference between the crypt counts following all three schedules over at least the first 2000 rad, a common line was drawn which was also a reasonable fit for the whole of the data from schedule A. The dotted line shows the curve published previously (Hamlet *et al.*, 1976) for the effect of single doses of γ irradiation.

Clearly schedule A produced a minimal reduction in numbers of regenerating crypts from 122±10 in control mice to 96±12 after ten fractions of 300 rad plus a 900 rad assay dose; a total of 3900 rad delivered over a period of 12 days and assayed 3½ days later at 15½ days. By contrast, a similar total dose of 4000 rad with schedule C reduced the crypt count to 33±3 with an even lower score of 18.5±6 after 4250 rad over six days, assayed at 9½ days. A small, but significant reduction in crypt number to 85±5 occurred with schedule B after daily fractions of 450 rad in four days, assayed at 7½ days. These three dose-response curves will be referred to individually to enable comparison to be made with the relevant scanning electron microscopical appear-

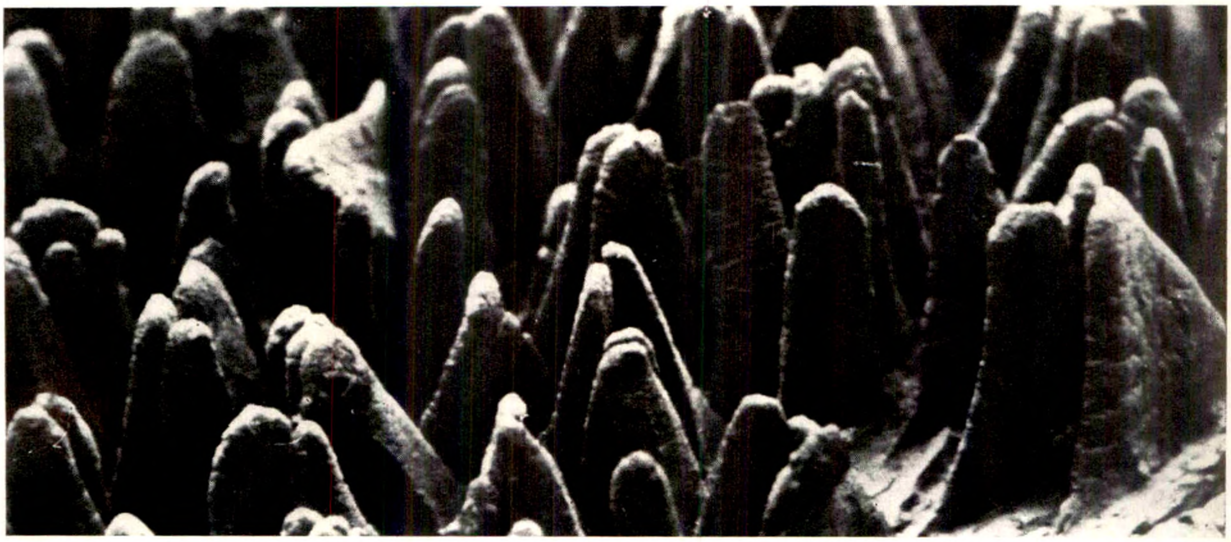

Fig. 2a.

Scanning electron micrograph (SEM) of mouse ileum. This is a control of good quality showing well preserved finger-like villi. (×200)

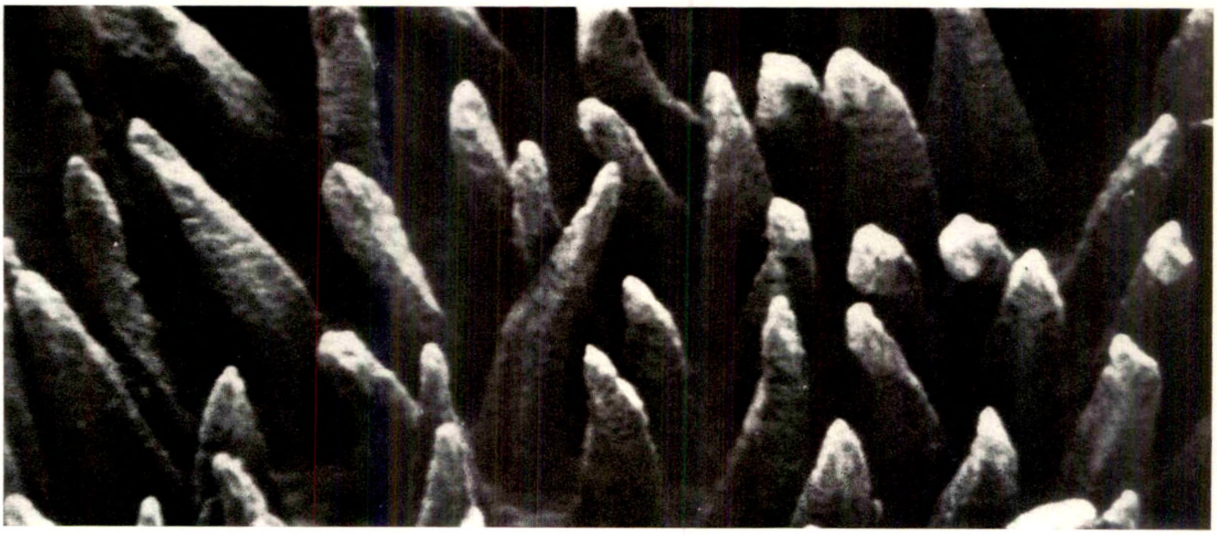

Fig. 2b.

SEM of control chosen for its relatively poor quality. (×200) ance of the villi of replicate samples of jejunum from the same mice.

Hendry and Potten (1974) have shown that regenerating crypts three days after single doses of irradiation appear larger than normal crypts. Thus they would have a greater probability of appearing in a section of intestine. For accurate assessment of D_0 and extrapolation number, particularly after crypt survival data are transformed into values of cell survival, they suggest that a correction factor of 0.88 be applied to crypt results obtained from irradiated intestine. As we have found no significant difference between crypt counts from control animals and those given low doses in our experiments, and because we are not using a conversion to cell survival and also because the crypt results are being used principally for comparison between and within fractionation schedules, we have decided that it was not necessary to use a correction factor for the presentation of our crypt survival data.

Scanning electron microscopy

In all three schedules, the scanning electron micrographs showed an unevenness in the progression of surface damage with increasing dose and in some cases a variation in the damage seen in samples from different animals which had received the same dose. There was also a variation in the appearance of the control specimens, as seen in Figs. 2A and 2B. In order to assess these varying results, seven different factors influencing the morphology of the villi were chosen and the whole area of each of the micrographs from each piece of gut was assessed independently for each of these factors (Figs. 2–6 illustrate only part of each area).

The factors were: apparent villus height, apparent width, separation of the villi, erectness of the villi, contours of the villus tips, clumping of the villi and finally creasing of the villus surface with accompanying surface damage such as wartiness or blebs. Height and width of villi were included in this subjective assessment since the problems raised by the disorientation, twisting and kinking of unsupported specimens were such that accurate measurements were not possible.

Each factor was scored on a ranking system, from one to eight. One represented the "ideal" appearance of this factor, such as would be seen on a well preserved control specimen (see Fig. 2A). Two and three represented minimal and slight damage and four and five indicated moderate and substantial damage respectively. Six, seven and eight were used to indicate the range of severe to gross damage seen in some samples at the end of the experimental schedules.

The mean scores for each factor were obtained from the scores from the individual specimens. For any given dose, the mean scores for all factors were then added together to give a total which could then be used as an index of the cumulative damage. Initially, the scores have been represented as a compound histogram, which includes the control

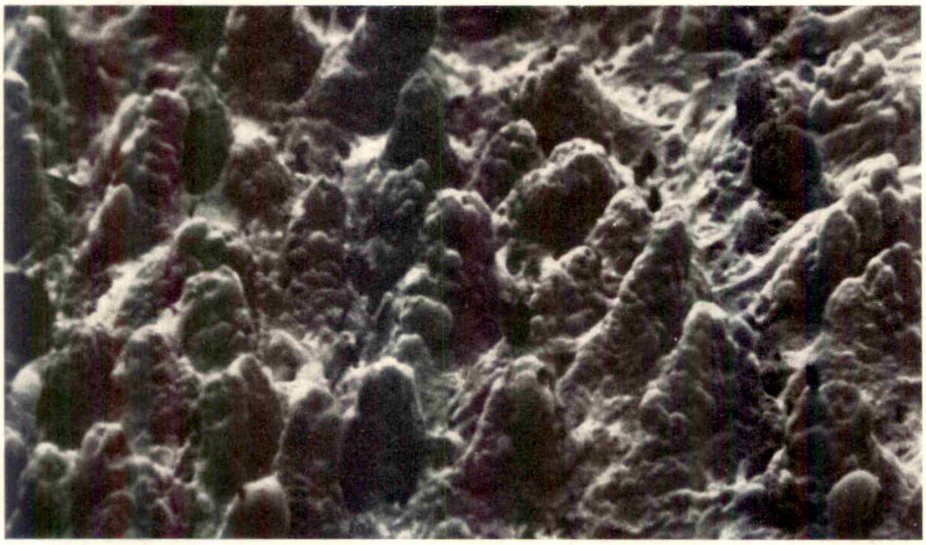

FIG. 3.

SEM from schedule A. Total dose 3000 rad. The villi are badly damaged, stumpy in shape and with abnormally bumpy surface. (× 200)

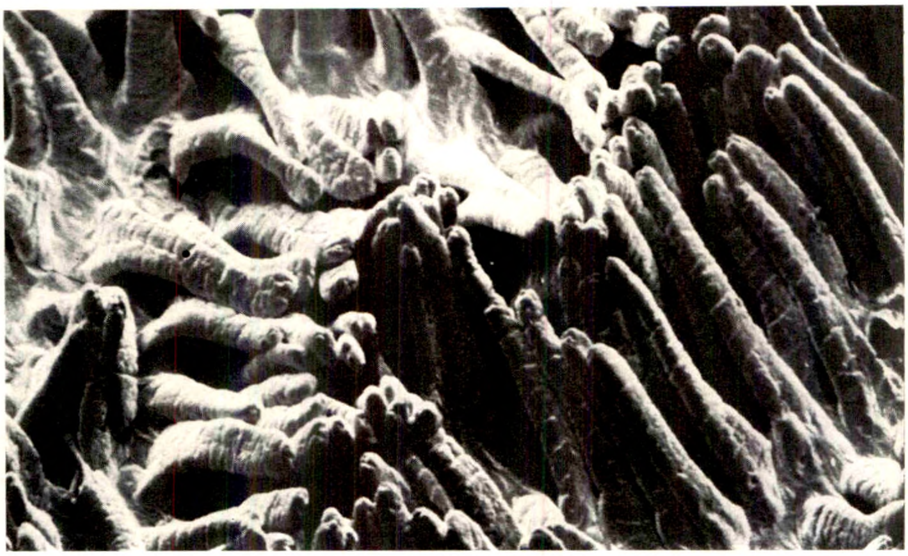

FIG. 4.

SEM from schedule B. Total dose 2250 rad. The villi are fairly normal with a change in apparent height, i.e. they appear longer and floppy. They are not, however, badly damaged. (×100)

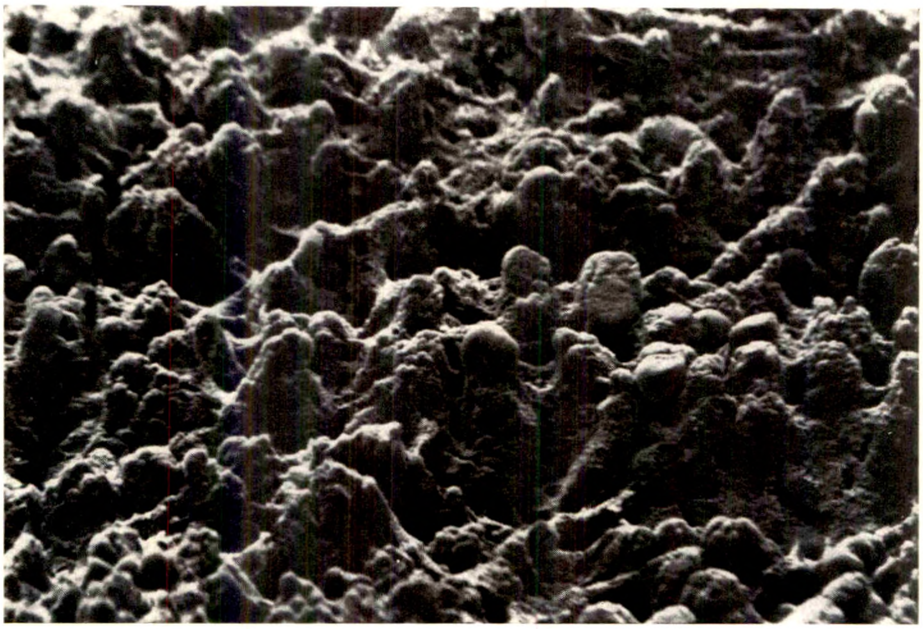

FIG. 5.

SEM from schedule C. Total dose 4250 rad. The villi are badly damaged with a very warty surface and blebs at some of the tips. (×100)

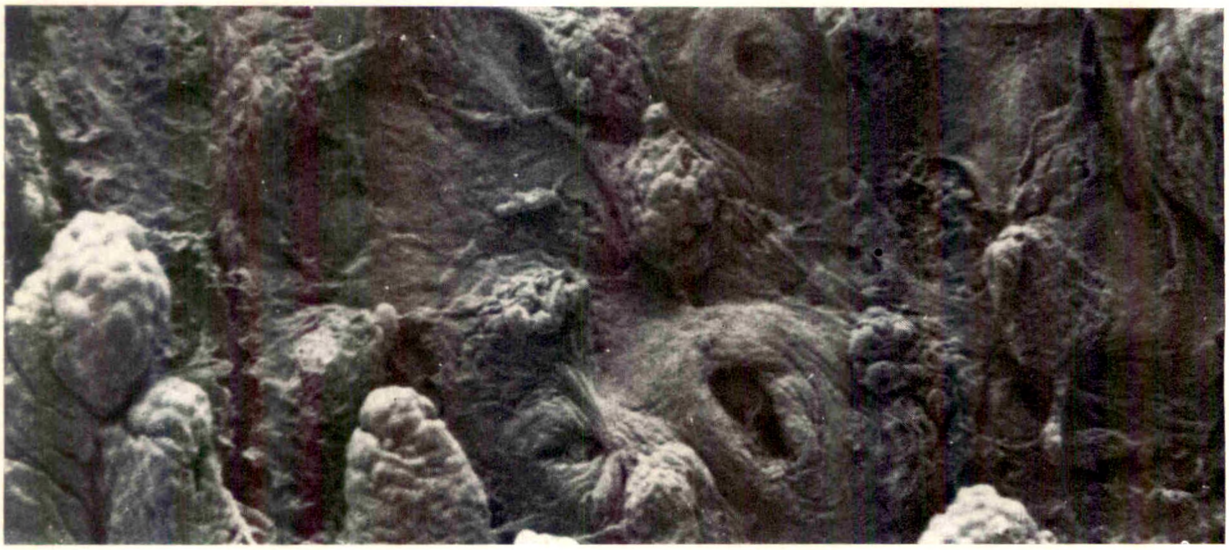

FIG. 6.

SEM from schedule C. Total dose 3750 rad. Sample of irradiated gut showing signs similar to those seen with coeliac disease. (×200)

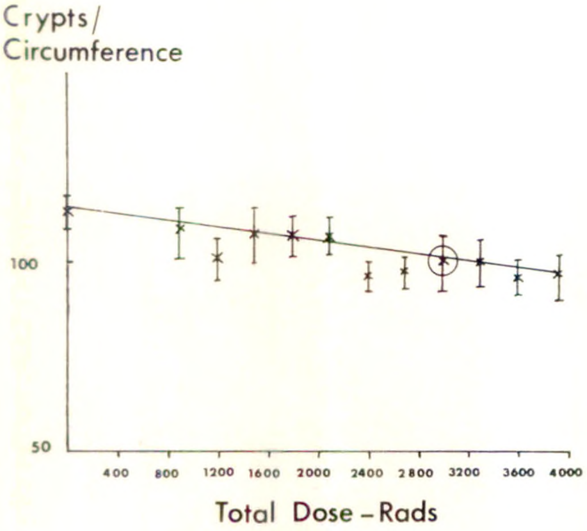

FIG. 7A.

Crypt survival curve for schedule A. Circle refers to the sample shown in Fig. 3.

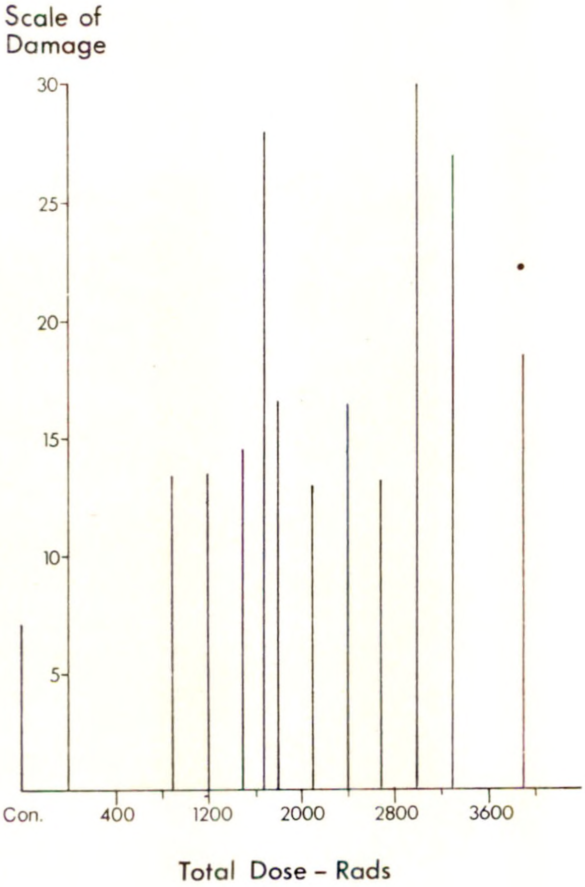

FIG. 7B.

Histogram of surface damage in schedule A as illustrated by scanning electron micrography.

and varies as the schedules continue, from a minimum of seven upwards.

The compound histograms for the three schedules are shown, with the relevant graph of crypt counts, in Figs. 7, 8 and 9. The doses illustrated in the scanning electron micrographs (Figs. 3–5) are marked on the crypt count graphs. This allows the individual micrographs to be examined in context with the damage observed throughout the schedule, as seen by crypt counting and scanning microscopy.

The damage seen by scanning microscopy as interpreted through the histograms is described below for each schedule.

Before showing the results of irradiation, two examples of jejunal mucosa from untreated mice are provided in Fig. 2 to illustrate the fact that there are variations in the appearance of the villi but that these are relatively slight when compared with the pictures of gut from irradiated mice (Figs. 3–6). Using the semi-quantitative scoring system the upper example (Fig. 2A) would score only seven while the lower (Fig. 2B) would score nine—a slightly higher number but well below the values of 13–30 to be given later for samples of gut from irradiated mice. The main difference between these two control samples lies in the fact that the villi are less erect in the lower example but the appearances are otherwise very similar.

Space only permits one photograph of gut sampled from each of the three fractionation régimes and these have therefore been selected to illustrate the broad conclusions of this report. The semi-quantitative SEM assay has, however, been performed using photographs of at least four samples at each dose level, as has quantitative crypt counting, and all these data are shown in Figs. 7–9 in order to make it quite clear how representative Figs. 2–5 are. Thus Fig. 3 shows the surface appearance of gut from a mouse which had received 3000 rad under schedule A. In Fig. 7A the appropriate crypt survival curve shows that the specimen was from a group with a mean count of 96 crypts. The histogram in Fig. 7B shows that the semi-quantitative score of villus damage was 30 after this dosage of fractionated radiation. Comparison of Figs. 3 and 7 shows considerable damage to the mucosal surface

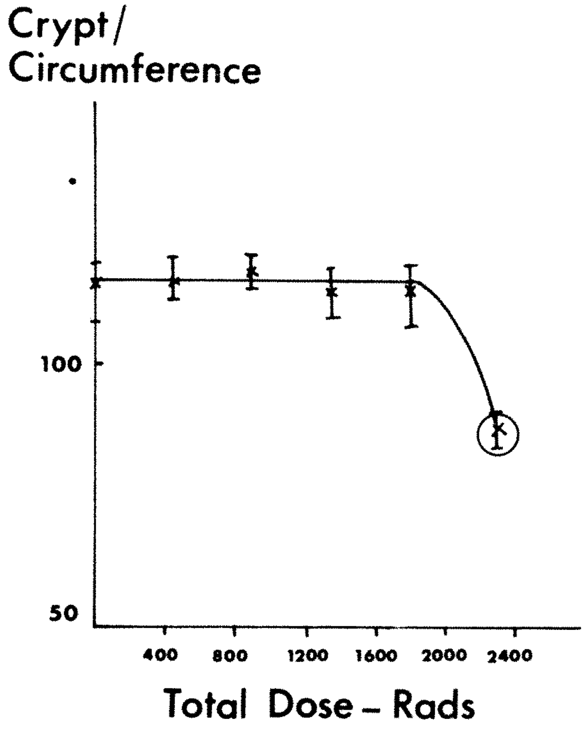

FIG. 8A.

Crypt survival curve for schedule B. Circle refers to the sample shown in Fig. 4.

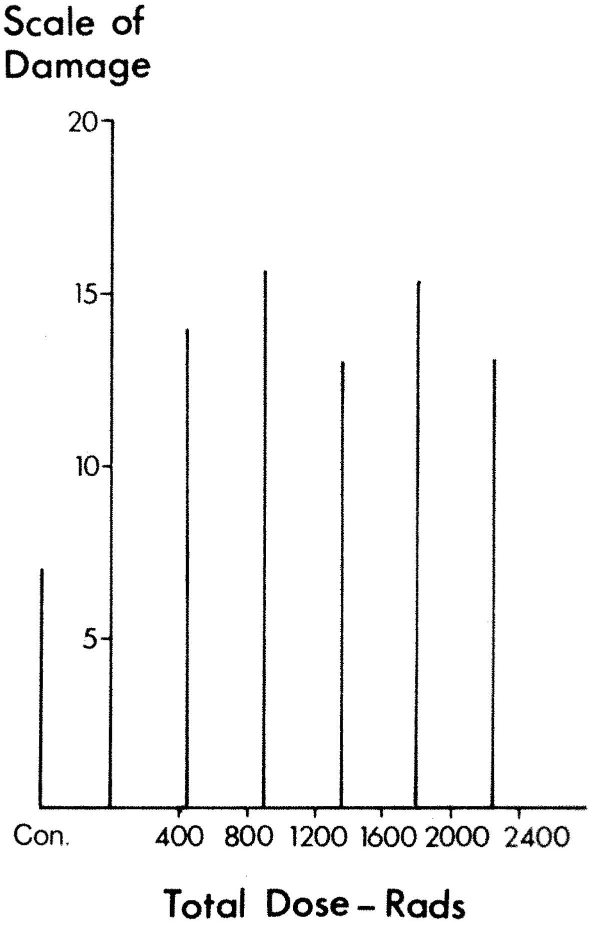

FIG. 8B.

Histogram of surface damage in schedule B.

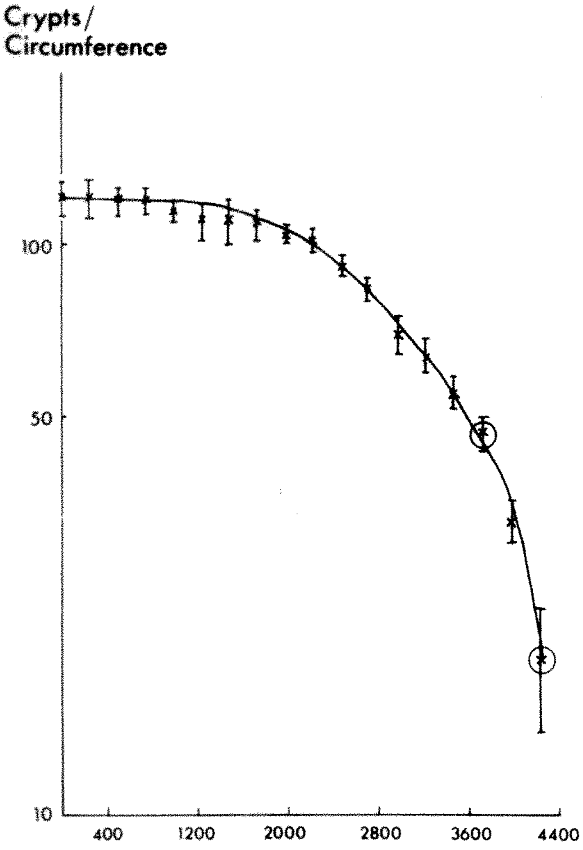

Fig. 9A.

Crypt survival curve for schedule C. Circle refers to the sample shown in Fig. 5.

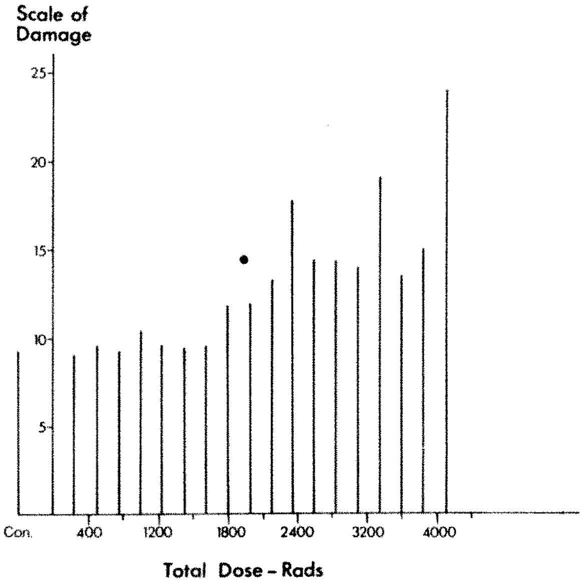

Fig. 9B.

Histogram of surface damage in schedule C.

with one of the highest scores on our assay system, in contrast to the minimal depression in crypt counts from 122 ± 10 to 96 ± 12, a difference which is hardly significant.

The crypt counting value corresponding to the sample of gut shown in Fig. 4 is significantly depressed, however, at 85 ± 5 (see Fig. 8A). On the other hand, the villus appearance scores only 13 on the semi-quantitative assay (Fig. 8B) and the SEM picture (Fig. 4) shows that a dose of 2250 rad under schedule B has caused only minor damage to the mucosa. The villi are clumped together and less erect but appear to have a greater than normal height. A small amount of villus damage can thus be correlated with a small depression in crypt regeneration after schedule B.

With schedule C there is also a good correlation between the results of the two assay methods. Figure 5 shows a very badly damaged mucosal surface in the SEM photograph after a total dose of 4250 rad which reduces crypt survival to only 18.5 ± 6 with a villus damage score of 24 (see Fig. 9). This does not represent as much surface damage as that shown in Figs. 3 and 7B (schedule A) but there is a reasonable correlation between the two scores in that a low crypt number is associated with a high villus damage number following a large total dose of radiation.

At the lower total dose of 3750 rad with this schedule a reasonable correlation is also found; namely, a crypt count of 47 ± 3 and a villus damage score of 14. A specimen from an animal which received this dose is shown in Fig. 6 and illustrates another variation sometimes found in the surface appearance. In this example the pattern is similar to that of coeliac disease with a localized absence of villi and a heaping up of cells around the mouths of the crypts.

Discussion

It is well known that intestinal epithelium is one of the cell-renewal populations, with stem cells in the crypts of Lieberkuhn proliferating to provide renewed cells which transit up onto the villus surface to be finally extruded from the tip. It follows from this that the response to radiation will be initially seen in the crypts as an inhibition of cell proliferation, followed in due course (depending on the transit time) by a reduction of villus cell population and therefore of villus height. It would therefore be expected that in a fractionation régime extending over a period of time much in excess of the transit time of the intestinal cell population from crypt to villus tip, the extent of crypt damage would be reflected in the amount of villus damage and vice versa. This expectation was confirmed by our data with treatment schedule C but not with schedule A and only to a small extent with schedule B.

Much of the radiobiological literature concerning the radiation response of small intestine is based upon the regenerating crypt counting method of Withers and Elkind (1970)—the so-called microcolony assay. Use of the method has provided detailed dose-response data for both single and fractionated radiation schedules but the authors (Withers *et al.*, 1976) make the assumption that the response of the jejunal mucosa is dependent upon the capacity of crypt stem cells to repair sublethal radiation injury and to regenerate. Over the range of doses used in our experiments, for example, they conclude that surviving crypt cells shed sublethal damage equivalent to about 60% of each dose. That leaves a residual damage of only 40% which, at the low dose levels in question, would easily be repaired by the regeneration consequent upon the two doublings per day from the 12 hour cycle time of the normal jejunal stem-cell population.

This hypothesis is confirmed by those authors' own experiment where mice received 275, 300 or 325 rad per day for nine days and a final dose of 1230 rad on the tenth day (a very similar régime to our schedule A). They concluded that crypt cell numbers were probably not depleted after such a régime and this is what we also found. Neither these authors nor others who use the microcolony assay make any observation on the effect on the villus surface of such régimes, however. The serious and even lethal effect of villus denudation is assumed to correlate with severe crypt damage but the present studies show that this may not always follow. The alternative end-point of gastrointestinal death does not necessarily provide a correlation either (Wambersie *et al.*, 1974) because such data were based upon the simple end-point of death (or survival) which does not permit much resolution of the degree of damage to the mucosal surface.

All these data from the literature and from our own experiments confirm the importance of damage to the intestinal mucosa in limiting the dosage of radiotherapy delivered in various fractionation régimes. The majority of studies concern the acute effects of radiation on gut. Late complications of radiotherapy have also been reported (Roswit *et al.*, 1972) and the radiological changes may mimic the effects of coeliac disease (Wellwood and Jackson, 1973) and other malabsorption syndromes. This was exemplified in our example shown in Fig. 6, albeit from an acute reaction.

The timing of even the acute reaction may be critical in determining the survival of the mouse to a régime of irradiation. This is especially relevant to those fractionation régimes where the duration extends into the period when bone-marrow death may occur, a circumstance which is possible with total body irradiation (as in our schedules A and B) but less likely when only the abdomen is irradiated (as in schedule C).

These results emphasize the fact that doses which do not seriously disturb the proliferative capacity of a biological system might considerably disrupt its specific function which may, in turn, affect systems remote from the site of insult. Also, they demonstrate that damage to different sections of the same organ may occur at different times thus complicating the complete picture of radiation injury. The possibility that some of these effects seen by scanning electron microscopy may, in part, be the consequence of damage to the underlying stroma will be examined by transmission electron microscopy.

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REFERENCES

HAMLET, R., CARR, K. E., TONER, P. G., and NIAS, A. H. W., 1976. Scanning electron microscopy of mouse intestinal mucosa after cobalt 60 and D-T neutron irradiation. *British Journal of Radiology*, *49*, 624–629.

HENDRY, J. M., and POTTEN, C. S., 1974. Cryptogenic cells and proliferative cells in intestinal epithelium. *International Journal of Radiation Biology*, *25*, 583–588.

ROSWIT, B., MALSKY, S. J., and REID, C. P., 1972. Severe radiation injuries of the stomach, small intestine, colon and rectum. *American Journal of Roentgenology*, *114*, 460–475.

WAMBERSIE, A., DUTREIX, J., GUEULETTE, J., and LELLOUCH, J., 1974. Early recovery for intestinal stem cells, as a function of dose per fraction, evaluated by survival rate after fractionated irradiation of the abdomen of mice. *Radiation Research*, *58*, 498–515.

WELLWOOD, J. M., and JACKSON, B. T., 1973. The intestinal complications of radiotherapy. *British Journal of Surgery*, *60*, 814–818.

WITHERS, H. R., and ELKIND, M. M., 1970. Microcolony survival assay for cells of mouse intestinal mucosa exposed to radiation. *International Journal of Radiation Biology*, *17*, 261–267.

WITHERS, H. R., CHU, A. M., REID, B. O., and HUSSEY, D. H., 1976. Response of mouse jejunum to multifraction radiation. *International Journal of Radiation Oncology, Biology and Physics*, *1*, 41–52.

1979, *British Journal of Radiology*, *52* 494–498

OER and RBE for negative pion beams of different peak widths

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Abstract

Experimental data on survival curves for pion beams of different peak widths under aerobic and hypoxic conditions are reported. Metabolic depletion of oxygen by the Chinese hamster cells (line V79) was used to obtain hypoxia. The results indicate that the RBE at the beam entrance (plateau) is approximately 1.0. When the Bragg peaks were broadened to widths of 1.3, 7.8, and 10.5 cm (at the 80% dose level), the RBE (50% cell survival) at the peak centres was 1.7, 1.6, and 1.2, respectively. The OER at the entrance was 2.4 compared with about 2.9 for X rays. The OER was independent of the survival level at which it was measured. The OER at the peak centres at widths of 1.3, 7.8, and 10.5 cm was 2.1, 2.4, and 2.2, respectively. These results indicate that, although the RBE at the centre of the 10.5 cm wide peak was significantly lower than at the centres of the 1.3 and 7.8 cm peaks, the OER values are similar for all peak widths used in this study.

The biological effects of pions have previously been studied mostly at low dose rates (4 rad/min) and in beams with a narrow peak (approximately 1.5 cm in lucite at the 80% dose level) (Feola *et al.*, 1968; Loughman *et al.*, 1968; Raju *et al.*, 1970; Raju and Richman, 1972; Baarli and Bianchi., 1972; Dertinger *et al.*, 1976; Fritz-Niggli, 1976). The pion beam used by the group in Great Britain was from a high-energy physics facility at Harwell (NIMROD); it had a low dose rate (3 rad/min) but a broader Bragg peak (about 3 cm in lucite at the 80% dose level) which is still small compared with peak widths necessary for therapeutic applications (Winston *et al.*, 1973; Nias *et al.*, 1974; Lloyd *et al.*, 1975; Purrott, 1975; Coggle *et al.*, 1976; Mill *et al.*, 1976). Pre-therapeutic radiobiology programmes are progressing rapidly at Los Alamos, Vancouver, and Zurich, and pion beams with increasing dose rates over large volumes are becoming available. Radiobiological work with pions has been reviewed by Raju and Richman, (1972), Raju, (1974) and Raju *et al.* (1977). It is of interest to study parameters of therapeutic concern such as OER and RBE and how they vary with changes in peak width. Measurements of cell survival as a function of depth for pion beams when their Bragg peaks were broadened to different widths have been reported by Raju *et al.* (1977). In this report, we present data on survival using Chinese hamster cells (line V79) under aerobic and hypoxic conditions at the peak centres for pion beams with different widths of peak.

Materials and Methods

Cells

A technique similar to that of Hall and Lehnert (1973) was used. Chinese hamster cells (line V79) were used in these experiments. Stock cultures were maintained in exponential growth as monolayers in plastic tissue-culture flasks (Falcon 3024, 75 cm^2 growing area) at 37°C in a humidified atmosphere containing 5% CO_2 with 95% air. The nutrient medium used was BME (Gibco G-13) supplemented with 50U/ml potassium penicillin, 50μg/ml streptomycin sulphate, 1.5 μg/ml amphotericin B, and 10% fetal calf serum. About 4×10^6 cells were inoculated into each of four 250 ml Falcon plastic flasks on the day before the experiment. On the day of the experiment, the cells in exponential growth were harvested by trypsinization. Cells were exposed in plastic capsules made from 1 ml Falcon pipettes cut into 4.4 cm long pieces. The internal and external diameters of the pipettes were 2.9 and 4.6 mm respectively. One end of the pipette piece was heat-sealed using a soldering iron with a modified tip, and the sealed end was immersed in molten wax to cover any microscopic holes. A series of capsules were filled from the bottom with 0.2 ml at 3×10^6 cells/ml and another series of capsules with 0.2 ml at 3×10^4 cells/ml. After filling, the open ends were also heat-sealed and immersed in molten wax. The capsules were always kept in the vertical position to allow the cells to settle to the bottom. The capsules were kept in an incubator (37°C) for two hours and at room temperature (approximately 20°C) for about three hours. After this total period of five hours, the capsules with a concentration of 3×10^6 cells/ml were found to be radiobiologically hypoxic as judged by their X-ray response, and the capsules with a concentration of 3×10^4 cells/ml remained aerobic, as reported by Hall and Lehnert (1973). After exposure, the capsules were vigorously shaken for about one minute using a Yankee pipette shaker.* One end of the plastic capsule was cut using a single-edged razor blade. The cell suspension was pipetted about

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*Made by Clay Adams, Division of Becton-Dickinson and Company, Parsippany, N. J. 07054, USA ten times using a Pasteur pipette before the cells were removed from the capsule. After making appropriate dilutions, the cells were plated on Falcon plastic dishes and assayed for colony formation.

Radiation exposures

X rays generated at 250 kV (Thoraeus II filter) were used as a standard source for the control experiments. Exposures were made at room temperature using a vertical beam covering the entire length of the capsule. The capsules were kept at approximately a 45° angle during exposure so that the cells remained at the bottom.

Three pion beams were used in this investigation. The biomedical beam at the Los Alamos Meson Physics Facility (LAMPF) is a vertical beam and is nearly monoenergetic (momentum beam spread $\Delta P/P$ about 2%). The width of the Bragg peak is about 3 cm at the 50% dose level and 1.3 cm at the 80% level. This beam was modified to give peak widths of 7.8 and 10.5 cm (at the 80% dose level) using a dynamic range shifter (Amols *et al.*, 1977) which consisted of a fluid-filled piston that can be computer-programmed to modify the depth-dose distribution of a nearly monoenergetic beam to any desired peak width and shape. The plastic capsules were exposed to a series of doses at the peak centres of the three beams and at the entrance (plateau) of the beam with a 7.8 cm wide peak. The thickness of the capsule in the beam direction was 5 mm. The entire length of the capsule (about 4 cm) was within the 90% isodose contour.

Results

X rays

Previous experience indicated that keeping the capsules for two hours at 37°C and for about three hours at room temperature gave reproducible results. Storage at room temperature for up to 24 hours prior to exposure did not alter the sensitivity of either the aerated or hypoxic cells. Also, delays of up to three hours between exposure and plating of the cells did not result in significant differences in radiation sensitivity. The fact that the radiation sensitivity remains the same with storage at room temperature either before or after exposure makes this technique highly suitable for radiobiological studies at accelerators where occasional delays are inevitable.

The experiments using X rays were always done in parallel with pion experiments. A dose rate of 200 rad/min was used in most experiments. The results of all experiments pooled together are shown in Fig. 1. It can be seen that good hypoxia was obtained using this method. The OER of about three was found to be nearly independent of the dose level at which it was calculated; hence, oxygen appears to be a dose-modifying factor under these experimental conditions.

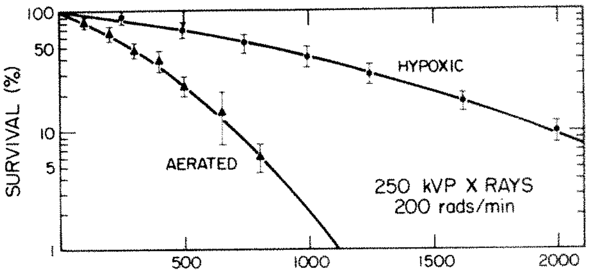

Fig. 1.

Percent survival *vs* dose of X rays for aerobic and hypoxic V79 cells. The points plotted represent the average of six different experiments, and the error bars represent one standard deviation (from the six experiments). The solid line represents the best fit to the data according to the Leenhouts-Chadwick model, as explained in the text.

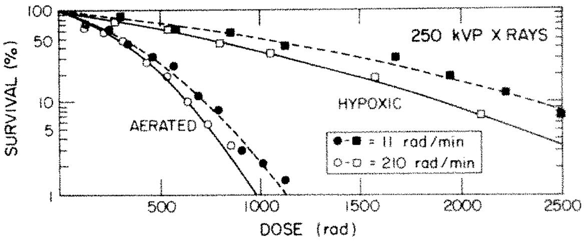

Fig. 2.

Percent survival *vs* dose for X rays at 11 and 210 rad/min under aerobic and hypoxic conditions.

X-ray cell survival measurements under aerated and hypoxic conditions were also made at dose rates of 11 and 210 rad/min to study the effect of dose rate on RBE and OER. As shown in Fig. 2, the data indicate that survival levels at low dose rates were slightly higher than at high dose rates (the difference may not be statistically significant) and that the OER does not vary by more than about 10% in this dose-rate region.

Negative pions

The aerobic and hypoxic capsules were exposed at the following positions in a lucite block: (1) entrance (plateau) (8 rad/min); (2) the centre of the peak 1.3 cm wide labelled A in Fig. 3 (25 rad/min); (3) the centre of the peak 7.8 cm wide labelled B (12 rad/min); and (4) the centre of the peak 10.5 cm wide labelled C (10 rad/min). The dose rates were measured using a thimble-type ionization chamber which was calibrated on a ^{60}Co γ-ray beam. No corrections for the values of W, stopping power, or kerma have been made since these factors are not known. Errors resulting from this approximation have been estimated to be 5% or less (Dicello, 1976). The depth dose distribution of pion beams and the points at which the exposures were made are shown in Fig. 3. Two experiments were done at each position. In order to minimize subjectivity in determining RBE and OER, a least-squares fitting routine was used to analyse the cell survival data according to the models of Wideröe (1968), $S=e^{-\alpha D}[1-(1-e^{-D/D_0})^n]$, and Leenhouts and Chadwick (1973), $S=e^{-\alpha D-\beta D^2}$.

The survival curves at each position are shown individually in Figs. 4–7. The solid lines through

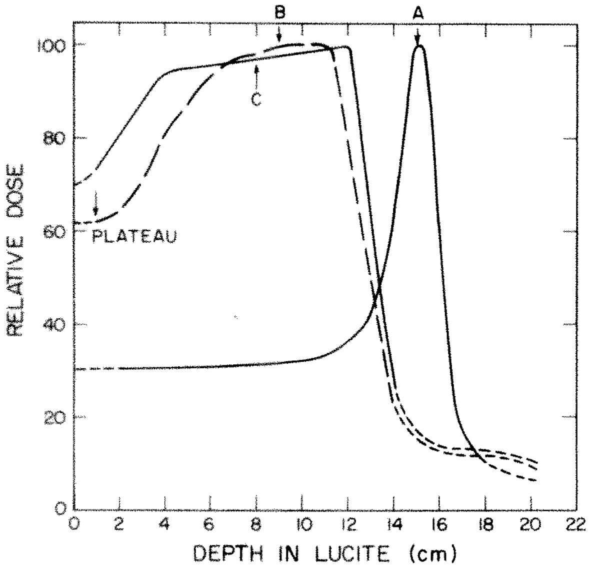

FIG. 3.

Relative dose *vs* depth for the three pion beams used in this experiment. The arrows indicate the positions at which cell irradiations were made. Curve A is for the unmodified pion beam; curves B and C were obtained by using a dynamic ridge filter. The peak widths at the 80% dose level for curves B and C were 7.8 and 10.5 cm in lucite respectively. The density of lucite is 18% greater than water.

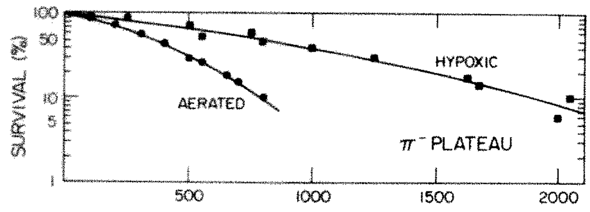

FIG. 4.

Percent survival *vs* dose of negative pions at the entrance position. The points plotted represent the average of two experiments. The solid lines represent the best fit to the data according to the Leenhouts-Chadwick model.

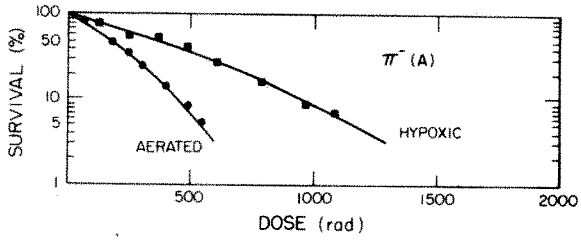

FIG. 5.

Percent survival *vs* dose of negative pions at the peak position of the unmodified pion beam (curve A, Fig. 3). The points plotted represent the average of two experiments. The solid lines represent the best fit to the data according to the Leenhouts-Chadwick model.

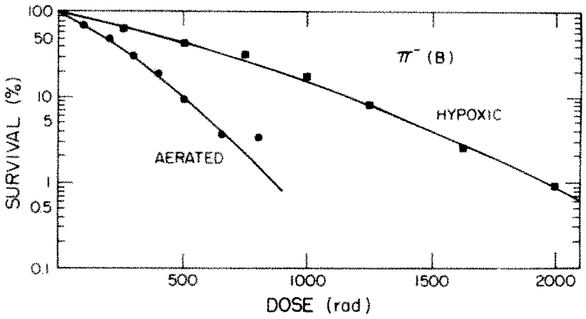

FIG. 6.

Percent survival *vs* dose of negative pions at the peak centre (curve B, Fig. 3). The points plotted represent the average of two experiments. The solid lines represent the best fit to the data according to the Leenhouts-Chadwick model.

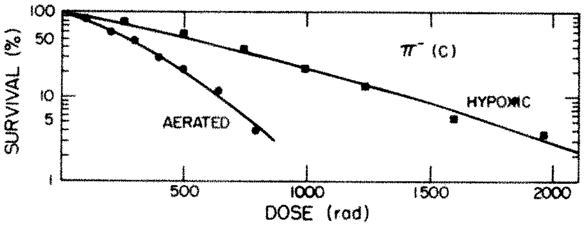

FIG. 7.

Percent survival *vs* dose of negative pions at the peak centre (curve C, Fig. 3). The points plotted represent the average of two experiments. The solid lines represent the best fit to the data according to the Leenhouts-Chadwick model.

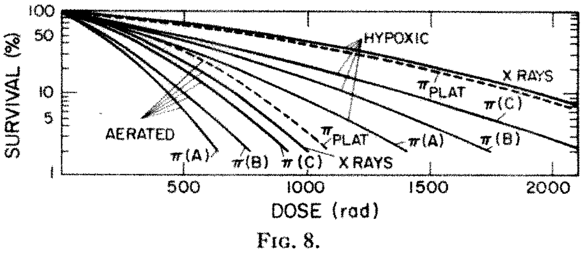

FIG. 8.

Percent survival *vs* dose for X rays (200 rad/min) and pions in the peak (curves A, B, and C in Fig. 3) and at the entrance (plateau). The curves represent the best fits to the data as described in the text.

TABLE I

LEENHOUTS-CHADWICK MODEL

Beam	α (rad$^{-1}\times10^3$)	β (rad$^{-2}\times10^6$)	RBE$_{50}$	RBE$_{10}$	OER$_{50}$	OER$_{10}$
X rays, air	1.8	2.1	1.0	1.0	3.0	2.8
X rays, hypoxic	0.5	0.3	—	—		
π^-, 1.3 cm peak, air	3.5	3.9	1.7	1.6	2.1	2.1
π^-, 1.3 cm peak, hypoxic	1.8	0.7	—	—		
π^-, 7.8 cm peak, air	3.5	2.0	1.6	1.4	2.4	2.3
π^-, 7.8 cm peak, hypoxic	1.4	0.5	—	—		
π^-, 10.5 cm peak, air	2.1	2.3	1.1	1.1	1.9	2.2
π^-, 10.5 cm peak, hypoxic	1.3	0.2	—	—		
π^-, 7.8 cm entrance (plateau), air	1.2	2.1	0.8	0.9	2.3	2.4
π^-, 7.8 cm entrance (plateau), hypoxic	0.6	0.3	—	—		

TABLE II

WIDERÖE MODEL

Beam	Initial D$_o$ (rad)	Final D$_o$ (rad)	$\frac{\text{Initial D}_o}{\text{Final D}_o}$	D$_Q$ (rad)	RBE$_{50}$	RBE$_{10}$	OER$_{50}$	OER$_{10}$
X rays, air	460	180	2.6	340	1.0	1.0	2.9	2.9
X rays, hypoxic	4000	640	6.3	560	—	—		
π^-, 1.3 cm peak, air	420	150	2.8	120	1.7	1.6	2.0	2.1
π^-, 1.3 cm peak, hypoxic	530	280	1.9	390	—	—		
π^-, 7.8 cm peak, air	300	160	2.0	170	1.6	1.4	2.2	2.4
π^-, 7.8 cm peak, hypoxic	630	300	2.1	650	—	—		
π^-, 10.5 cm peak, air	370	160	2.4	330	1.2	1.1	2.1	2.2
π^-, 10.5 cm peak, hypoxic	1600	490	3.2	290	—	—		
π^-, 7.8 cm entrance (plateau), air	1200	240	4.8	260	0.8	0.9	2.3	2.4
π^-, 7.8 cm entrance (plateau), hypoxic	1700	580	3.0	660	—	—		

these data points are the best fits using the model of Leenhouts and Chadwick. A composite of all survival curves without data points is shown in Fig. 8. The RBE and OER estimates at 50% and 10% survival calculated using both the Leenhouts-Chadwick and Wideröe models are shown in Tables I and II. Also included in Table I are values of α and β for the Leenhouts-Chadwick model and in Table II the values of initial slope, final slope, and shoulder width (D_Q) for the Wideröe model. Because of limitations in beam time, the survival data in some cases could not be extended to lower survival levels to reach the exponential region. Hence, the calculated values of D_0 from Wideröe's model and the β component in the Leenhouts-Chadwick model may not always be reliable. Nevertheless, the biological models fit the data quite well. In the dose range studied here, there were no significant differences in estimates of OER and RBE obtained by these models and the maximum variations from experiment to experiment did not exceed ±0.2.

DISCUSSION

The RBE at the peak centres of the 1.3 and 7.8 cm wide peaks is high but is reduced sharply at the centre of the 10.5 cm wide peak. The OER values for a pion beam of a given width do not vary significantly with the level of cell survival, indicating that the oxygen effect appears to be a dose-modifying factor for pions. The OER does not increase considerably with increasing peak width. The OER at the entrance (2.3 to 2.4) seems to be significantly lower than that for X rays (2.8 to 3.0), and this result is consistent with the findings of Winston *et al.* (1973).

The fraction of dose deposited by charged particles from stars decreases sharply with increasing peak width, with a concomitant reduction in high LET components. However, with increasing peak width (or stopping volume), the fraction of dose resulting from neutrons from stars increases, compensating somewhat for the decrease in LET. Schillaci and Roeder (1973) calculated that the percentage of dose deposited by neutrons from stars in stopping volumes of 0.01, 0.1, and 1 litre was 2, 10, and 20%, respectively. The pion beams with peak widths of 1.3, 7.8, and 10.5 cm used in this investigation had stopping volumes of 0.05, 0.08, and 0.16 litre respectively. Previous experimental data (Raju *et al.*, 1977) indicate that charged particles from stars influence the RBE to a large extent during the last few centimetres of the distal end of the broad peak. The RBE is reduced sharply toward the proximal end of the broad peaks where a larger fraction of the dose is due to ionization loss of passing pions, and the dose fraction from stars is considerably reduced. However, the increasing fraction of dose due to neutrons from stars with increasing peak width, as indicated by the calculations of Schillaci and Roeder, seems to be responsible for obtaining similar OER values for different peak widths. This is consistent with the work of Raju and Jett (1977) in which it was indicated that a small component of high LET radiation significantly decreases the OER without appreciably increasing the RBE.

As shown in Table II, the effect of negative pions on cells is mainly in reducing the width of the shoulder (D_Q) rather than in altering the final slope of the survival curve. In conclusion, our results indicate that, although the RBE at the centre of the 10.5 cm wide peak was significantly reduced when compared with centres of 1.3 and 7.8 cm peaks, the OER values are similar for all widths of peak used in this study.

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REFERENCES

Amols, H. I., Liska, D., and Halbig, J., 1977. The use of a dynamic range shifter for modifying depth-dose distributions of negative pions. *Medical Physics*, *4*, 404–407.

Baarli, J., and Bianchi, M., 1972. Observed variations of RBE values in the stopping region of a 95 MeV negative pion beam. *International Journal of Radiation Biology*, *22*, 183–186.

Coggle, J. E., Gordon, M. Y., Lindop, P. J., Shewell, J., and Mill, A. J., 1976. Some *in vivo* effects of π mesons in mice. *British Journal of Radiology*, *49*, 161–165.

Dertinger, H., Lücke-Huhle, C., Schlag, H., and Weibezahn, K. F., 1976. Negative pion irradiation of mammalian cells. I. Survival characteristics of monolayers and spheroids of Chinese hamster lung cells. *International Journal of Radiation Biology*, *29*, 271–277.

Dicello, J. F., 1976. Dosimetry of pion beams. In "*Particle Radiation Therapy, Proceedings of an International Workshop*," American College of Radiology, pp. 155–183.

Feola, J. M., Richman, C., Raju, M. R., Curtis, S. B., and Lawrence, J. H., 1968. Effect of negative pions on the proliferative capacity of ascites tumor cells (lymphoma) *in vivo*. *Radiation Research*, *34*, 70–78.

Fritz-Niggli, H., 1976. First biological experiments with the biomedical pion beam of the SIN. *Atom Kernenergie*, *27*, 181–186.

Hall, E. J., and Lehnert, S., 1973. The biophysical properties of 3.9 GeV nitrogen ions. IV. OER and RBE distributions using cultured mammalian cells. *Radiation Research*, *55*, 431–436.

Leenhouts, H. P., and Chadwick, K. H., 1973. Radiation induced DNA strand breaks and chromosome aberations. *Theoretical and Applied Genetics*, *44*, 167–172.

Lloyd, D. C., Purrott, R. J., Dolphin, G. W., and Reading, D. H., 1975. An investiagtion of the characteristics of a negative pion beam by means of induced chromosome aberrations in human peripheral blood lymphocytes. *International Journal of Radiation Biology*, *27*, 223–236.

Loughman, W. D., Feola, J. M., Raju, M. R., and Winchell, H. S., 1968. RBE of π^- beams in the Bragg peak region determined with polyploidy induction in mammalian cells irradiated *in vivo*. *Radiation Research*, *34*, 56–59.

Mill, A. J., Lewis, J. D., and Hall, W. S., 1976. Response of HeLa cells to irradiation with π- mesons. *British Journal of Radiology*, *49*, 166–171.

Nias, A. H. W., Greene, D., Major, D., Perry, D. R., and Reading, D. H., 1974. Determinations of RBE values for fast neutrons and negative π- mesons using frozen HeLa cells. *British Journal of Radiology*, *47*, 800–804.

Purrott, R. J., 1975. Chromosome aberration yields in human lymphocytes exposed to fractionated doses of negative π mesons. *International Journal of Radiation Biology*, *28*, 599–602.

Raju, M. R., 1974. The biological effects of negative pions. In "Proceedings of the XIIIth International Congress of Radiology," Madrid (October 15–20, 1973), International Congress Series No. 339, *Radiology*, *2*, 441–446.

Raju, M. R., and Jett, J. H., 1974. RBE and OER variations of mixtures of plutonium alpha particles and X rays for damage to human kidney cells (T-1). *Radiation Research*, *60*, 473–481.

Raju, M. R., and Richman, C., 1972. Negative pion radiotherapy: physical and biological aspects. *Current Topics in Radiation Research*, *8*, 159–233.

Raju, M. R., Amer, N. M., Gnanapurani, M., and Richman, C., 1970. The oxygen effect of π- mesons in *vicia faba*. *Radiation Research*, *41*, 135–144.

Raju, M. R., Amols, H. I., Bain, E., Carpenter, S. G., Dicello, J. F., Frank, J. P., Tobey, R. A., and Walters, R. A., 1977. Biological effects of negative pions. *International Journal of Radiation Oncology, Biology, and Physics*, *3*, 327–334.

Schillaci, M. E., and Roeder, D. L., 1973. Dose distribution due to neutrons and photons resulting from negative pion capture in tissue. *Physics in Medicine and Biology*, *18*, 821–829.

Wideröe, R., 1968. New concepts in radiobiology and radiotherapy. *Radiologia Clinica et Biologica*, *36*, 308–322.

Winston, B. M., Berry, R. J., and Perry, D. R., 1973. Response of *vicia faba* to irradiation with a beam of negative π mesons. *British Journal of Radiology*, *46*, 541–547.

1979, *British Journal of Radiology*, 52, 499–500 JUNE 1979

Technical note

Use of TLD in radiation protection survey of mobile mass-miniature radiography unit

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The value of large scale MMR surveys of populations has sometimes been questioned (Kitabatake *et al.*, 1973; ICRP, 1970), by considering the usefulness of the diagnostic information received from such surveys in relation to the potential hazards. In this connection it was considered desirable to carry out a radiation protection survey and measurements of dose received by the patients in a mobile MMR unit used under local conditions in India, applying TLD techniques.

MATERIALS AND METHODS

The survey was carried out inside a self-contained mass-miniature radiography unit. It is built on a 424 cm wheel-base chassis and accommodates an Escorts (India) X-ray set (100 mA, 100 kV, inherent filtration 0.5 mm Al equivalent) with a rotating anode of 0.8 × 1.8 mm focal spot and a straight hood Odelca camera type 70-VII-U (N.V. Optische Industrie, Holland). The X rays pass through a stationary grid 426 mm × 426 mm on to a slightly curved 40 cm × 40 cm fluorescent screen (green), the light from which is focused by means of a combination of lens and concave mirror onto a 70 mm film. The dark room is located inside the van beyond the camera in a direction opposite to that of the operator. A bench is provided along one side of the van near the camera and dark room. The distance from the tube-head to the camera is fixed (91.5 cm). The patient is positioned in front of the camera on a lift stand and the height is adjusted by an electrical switch such that the patient is centred with respect to the mark on the camera hood. The operator stands in one corner of the van behind a lead screen with a viewing lead glass. Scopix T2 (a fast orthochromatic film) and Agfa-Gevaert (India) developer are used.

In this study $CaSO_4$:Dy, procured from the Division of Radiological Protection, Bhabha Atomic Research Centre, Bombay, was used as TLD. 50 mg aliquots of the TLD phosphor were dispensed in gelatin capsules, and the capsules were stuck to the patient with cellotape at the centre of the entry and exit levels (after positioning of the patient) and near the gonads. For gonadal dose measurement, the same capsule was used in two series of 25 patients each to enable the dose to be integrated and measured accurately. (It was verified by phantom studies that the presence of the capsule with TLD did not leave an impression on the film). For the survey of radiation levels inside the van, TLD capsules were stuck on the inside of the van at a height of 1.5 metre on the door frame near the hinges of the entry and exit doors. Similar TLD capsules were also stuck on the patient side and the operator side of the lead glass viewing window of the protective screen, on the bench and on the outer walls of the van. Both the entry and exit doors were kept open during the exposure. After exposures the doses were evaluated by a Harshaw TLD-2000 reader.

In view of its well-known energy dependence, particularly at low energies, calibration of the $CaSO_4$:Dy phosphor was done against a Siemens dosimeter with a soft radiation chamber. This chamber is intended for measurement of soft X rays where the error does not exceed ±2% for the entire range 12–80 kVp. An additional check was carried out by comparing the Siemens dosimeter values with film dosimetry with the kind co-operation of the Bhabha Atomic Research Centre. The results agreed within ±5%.

A chest phantom (simulating lung tissue, bone and soft tissue in appropriate composition and anatomy) was fabricated and used to arrive at the optimum settings of filtration and mAs which would give good quality radiographs consistent with minimum radiation exposure. The current setting chosen was 20 mAs with 1.6 mm added Al filter (total filtration 2.1 mm Al). Depending upon the thickness of the patient three different settings of kVp were used, viz. 70, 76 and 80. The total number of patients studied was 50 (all adult males).

TABLE I

ENTRY AND EXIT EXPOSURES RECEIVED BY PATIENTS UNDERGOING CHEST X-RAY BY MASS-MINIATURE RADIOGRAPHY UNIT

kVp	mAs	Total filtration mm Al	Total No. of cases studied	Mean Entry Exposure mR		Mean exit exposure mR
				Experimental	Calculated from table*	
70	20	2.1	20	170±12	178±7	2.5
76	20	2.1	15	231±13	217±7	4.0
80	20	2.1	15	256±29	254±11	5.0

*Radiological Health Handbook (1970).

TABLE II

RADIATION PROTECTION SURVEY OF MASS-MINIATURE RADIOGRAPHY VAN

Location of TLD dosimeters	Dose in mR per exposure
Entrance door	0.40
Exit door	0.70
Viewing (lead) glass on patient's side	1.4
Viewing (lead) glass on operator's side	Background
Bench	3.3
Outer walls of van	Background

RESULTS

Table I gives the mean values of entry and exit exposures for the three kVp settings used. For comparison the values derived from the tables in the Radiological Health Handbook (1970) are also included. The two sets of values are in close agreement.

The average male gonadal dose was 0.33 mR per exposure (average of two sets of integrated exposures).

Table II gives the radiation levels at the different locations inside the mass-miniature radiography van.

CONCLUSION

It may be seen from Table II that the dose per exposure at the bench is on the high side (3.3 mR) indicating that the screening between this area and the camera is inadequate. It would, therefore, be inadvisable for a person to be present in this area while exposures are being made. The unprocessed films should also not be stored in this region so as to avoid any fogging.

The present study has shown that the use of TLD is a convenient and sensitive method for the assessment of doses to the patient and operating personnel in MMR units. Keeping in view the utility of the MMR units in India, particularly in rural areas, for the diagnosis of chest diseases (even in the present survey two out of the 50 chest X-rays had doubtful shadows which were confirmed on further investigation to be tuberculosis cases), and the acceptable levels of radiation doses (150–330 mR per exposure as per the present survey), it is considered that mass-miniature radiography has a role to play under certain conditions.

ACKNOWLEDGMENTS

Our thanks are due to Brig S. K. Mazumdar, former Director, and Colonel B. R. Kochkar, Director, for their interest and encouragement. The chest phantom was designed and fabricated by Mr. R. Singh. The technical assistance provided by Sub. N. K. Ghosh in the operation of the mass-miniature radiography unit is gratefully acknowledged.

REFERENCES

ICRP 1970. Protection of the patient in X-ray diagnosis, *Publication, 16*, pp. 13–17 (Pergamon Press).

KITABATAKE, T., YOKOYAMA, M., SAKKA, M., and KOOA, S., 1973. Estimation of benefit and radiation risk from mass chest radiography. *Radiology, 109*, 37–40.

Radiological Health Handbook 1970, compiled and edited by the Bureau of Radiological Health and the Training Institute, Environmental Control Administration, pp. 158–160, (U.S. Department of Health, Education and Welfare, Superintendent of Documents, Government Printing Office, Washington DC 20402, USA).

1979, *British Journal of Radiology*, *52*, 501–502

JUNE 1979

Case reports

Tricuspid endocarditis complicating pacemaker implantation demonstrated by echocardiography

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(*Received August, 1978*)

Tricuspid valve endocarditis is uncommon and as a complication of pacemaker implantation it is rare. A patient in whom this occurred is described. Echocardiography showed the presence of tricuspid valve vegetations which regressed following antibiotic treatment.

CASE REPORT

A 56-year-old man with a two year history of Stokes Adams attacks had a pacemaker implanted in September 1970. Elective replacement in January 1974 was uneventful. In October 1976 he was admitted to hospital with bradycardia of 30 beats/min. A temporary transvenous endocardial electrode was inserted via the left median cubital vein. The permanent pacemaker and electrode were explored on October 28 and the electrode was found to be faulty. Replacement of this was technically difficult and the procedure took almost four hours. During this period ventricular fibrillation occurred twice but promptly responded to direct current defibrillation. Eventually stable pacing was achieved and a permanent pacemaker implanted in the right pectoral region. Antibiotic prophylaxis was given: ampicillin 250 mg q.d.s. and flucloxacillin 250 mg q.d.s. for six days. He was discharged after removal of sutures on the seventh day. The wounds were healed and clean. On 13.12.76 pacing was satisfactory and the wounds were again noted to be clean.

On 6.1.77 he was admitted to hospital with a four day history of malaise and rigors. He was confused and pyrexial (maximum temperature 40°C). A systolic murmur, not previously noted, was heard in the tricuspid area. The spleen was palpable 3 cm below the left costal margin. A diagnosis of tricuspid valve endocarditis was suspected. Two blood cultures taken on the day of admission grew gram positive cocci and treatment with fucidin 500 mg t.d.s. and lincomycin 1.2 G b.i.d. was commenced. On 10.1.77 pacing was only intermittent and on 13.1.77 epicardial pacing was instituted via the xiphisternal approach; a new pacemaker was implanted in the anterior abdominal wall. The right pectoral pacemaker and electrode were removed.

On 14.1.77 he became more confused and was hypotensive: septicaemic shock was diagnosed. He received solumedrone 2 G stat and 500 mg q.d.s., fucidin 500 mg t.d.s. and gentamicin 80 mg t.d.s. lincomycin was stopped because of diarrhoea. On 15.1.77 he bacame unconscious and oliguric. Haemoglobin had fallen from 14.1 g/dl to 9.3 g/dl and blood urea had risen from 11.3 m.mol/l to 32.8 m.mol/l Peritoneal dialysis was commenced using Diaflex No. 61 solution. Echocardiography showed vegetations on the anterior cusp of the tricuspid valve and a small pericardial effusion (Fig. 1A).

He remained seriously ill for two weeks: recovery was complicated by a right deep vein thrombosis and severe pulmonary oedema. Gradually he began to improve; urine output increased and blood urea began to fall. On 23.2.77 echocardiogram of the tricuspid valve was normal (Fig. 1B). Intermittent peritoneal dialysis was continued and further recovery was uneventful. He was discharged on 6.4.77. The blood urea was normal.

The blood glucose was elevated on several occasions and he was subsequently shown to be mildly diabetic. This was adequately controlled by dietary restrictions.

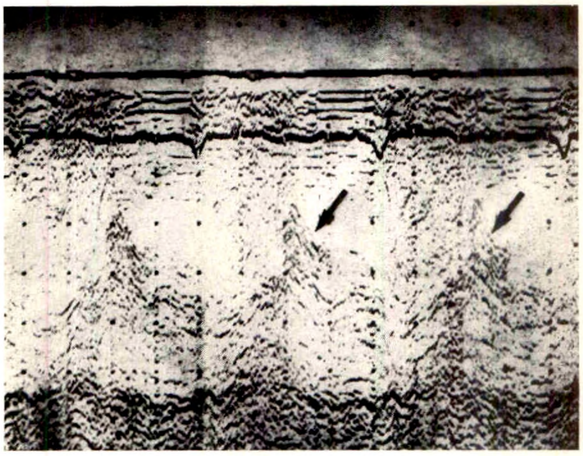

FIG. 1A.

Tricuspid endocarditis. Vegetations (arrowed) are superimposed as multiple echoes on the trace of the tricuspid valve.

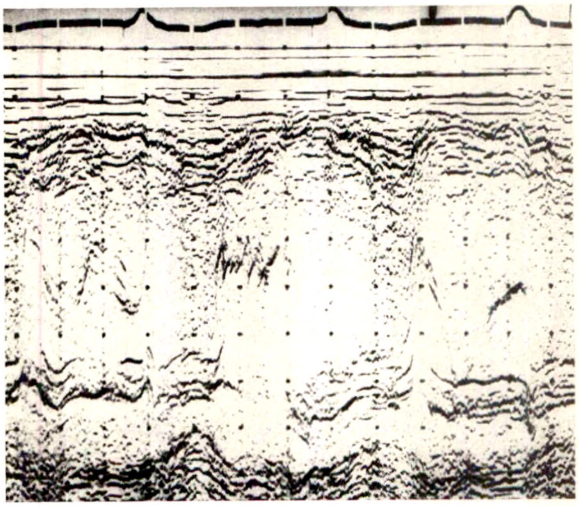

FIG. 1B.

Trace of the tricuspid valve following treatment. Thin cusp echoes are seen.

1979, *British Journal of Radiology*, *52*, 502–504

DISCUSSION

Infective endocarditis is a rare complication of pacemaker implantation (Schwartz and Pervez 1971). Two factors contributed to its occurrence in our patient. Firstly, the length of time taken to implant the new unit and also diabetes mellitus (Torresani *et al.*, 1969). The diagnosis was established by clinical findings, echocardiography and positive blood culture. Echocardiography readily demonstrates vegetations on the aortic and mitral valves but convincing examples of tricuspid valve vegetations are uncommon. This is because of the difficulty of obtaining clear tracings of even the normal tricuspid valve and the rarity of tricuspid endocarditis. Vegetations are seen as fuzzy, speckled echoes superimposed on the valve cusps (Fig. 1A). In this case, the ultrasound confirmed the clinical diagnosis but echocardiography may also help in the diagnosis of endocarditis when the blood cultures are negative (Naik *et al.*, 1978).

REFERENCES

NAIK, D. R., WARD, C., and HARDISTY, C. A., 1978. The role of echocardiography in suspected infective endocarditis. *Clinical Radiology*, *29*, 381–385.

SCHWARTZ, I. S., and PERVEZ, N., 1971. Bacterial endocarditis associated with a permanent transvenous cardiac pacemaker. *Journal of American Medical Association*, *218*, 736–737.

TORRESANI, J., BERNARD, Y., MONTIES, J. R., and JOUVE, A., 1969. Clinical experience in transvenous and myocardial pacing. *Annals of New York Academy of Sciences*, 167, 995–1007.

Ureteric changes in polyarteritis nodosa

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(*Received November, 1978*)

Polyarteritis nodosa is a collagen vascular disease manifesting itself as a necrotizing arteritis of small and medium-sized arteries. The kidneys are often radiographically involved and have been well described in the literature. There are, however, only three case reports of ureteric changes associated with polyarteritis nodosa (Fisher and Howard, 1968; Samellas, *et al.*, 1971; Glanz and Grunebaum, 1976). This report adds a fourth case to the literature and also includes follow-up studies showing regression of the ureteric changes after steroid treatment.

CASE REPORT

A 19-year-old Japanese-American male was admitted to the hospital because of gastroenteritis with fever, vomiting and constant abdominal pain of three days' duration. Subsequent history of weight loss, migratory polyarthralgia, fever and chills for the preceding one-and-a-half months raised the question of more serious disease. There was no history of medication or drug abuse. Past history was otherwise unremarkable. Physical examination showed only non-specific mild epigastric tenderness. Laboratory findings included microhaematuria, slightly elevated white blood cell count and marginal elevation of alkaline phosphatase and liver enzymes.

Intravenous cholangiogram, oral cholecystogram, upper gastrointestinal and small bowel study and barium enema were all normal. An excretory urogram showed that the kidney and bladder were normal. The major finding was nodular irregularity with imprinting along the wall of the proximal right ureter, and fullness of the collecting system and renal pelvis on the right. There was also minimal irregularity of the proximal left ureter. Retrograde pyelography (Fig. 1) confirmed the IVP findings. Urine culture and cytology obtained during the retrograde examination were both negative.

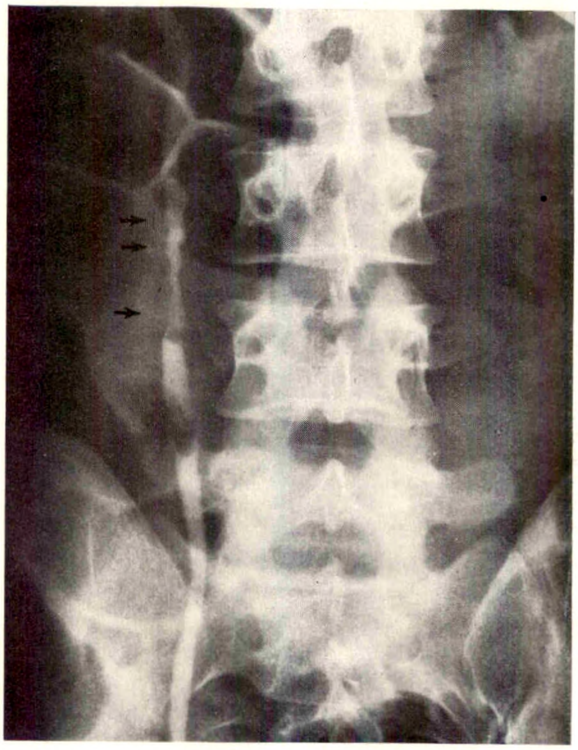

FIG. 1.

Retrograde examination of the right ureter shows irregularity.

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Because of persistent fever and right upper quadrant pain, the patient underwent exploratory laparotomy. At surgery the gall-bladder was inflamed, and a cholecystectomy was performed as well as an appendectomy. The proximal right ureter was thick-walled, indurated and inflamed. Biopsies taken in this area showed segmental necrotizing arteritis in the periureteric tissues. Similar changes were seen in the gall-bladder and appendix. Subsequent arteriography showed the liver, pancreas and bowel to be unremarkable. Microaneurysms were present in the distal small vessels of the kidneys bilaterally, particularly on the right (Fig. 2).

The patient's subsequent hospital course was unremarkable. He was discharged on steroid therapy. A follow-up excretory urogram two months later showed that the notching of the proximal right ureter was less marked, but there was still mild obstruction of the proximal urinary system. An excretory urogram one year later when the patient was in clinical remission showed the right ureter was now completely smooth and the mild obstruction was no longer present (Fig. 3).

DISCUSSION

Polyarteritis nodosa is a systemic disease which affects small and medium-sized arteries leading to functional impairment of organs. The disease is clinically manifested by various symptoms which depend on the location of the vascular lesions. Lesions are common in the kidneys, lungs, heart, gastrointestinal tract, liver and testes.

The kidneys are frequently involved and the angiographic findings in polyarteritis nodosa have been well described. Co-existence of distal microaneurysms with vascular irregularity and thrombosis is said to be specifically indicative, at least up to 80% of the time, of polyarteritis nodosa (Ekelund and Lindhold, 1974; Padovani, *et al.*, 1974).

Descriptions of ureteric lesions, such as were present in this case, are rare. The ureteric irregularity along with the mild obstructive changes seen on the excretory urogram are similar to those previously described. Thickening and oedema of the ureter walls caused by the involvement of the arteries in the circular muscular layer and in the adventitial connective tissue are responsible for the radiographic manifestations of irregularity and mild obstruction of the ureter. The follow-up excretory urograms demonstrate the reversibility of these ureteric changes.

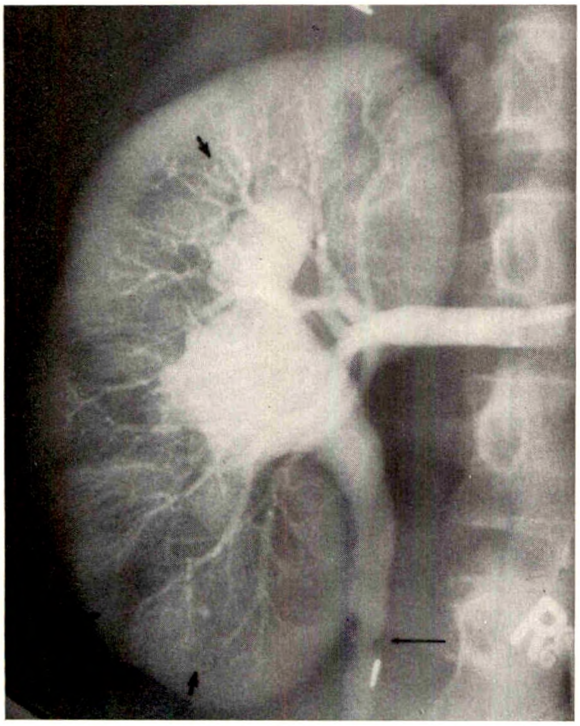

FIG. 2.

Magnification selective renal arteriograms demonstrating microaneurysms (short arrows). Also note irregularity of proximal ureter (long arrows), and fullness to collecting system and pelvis.

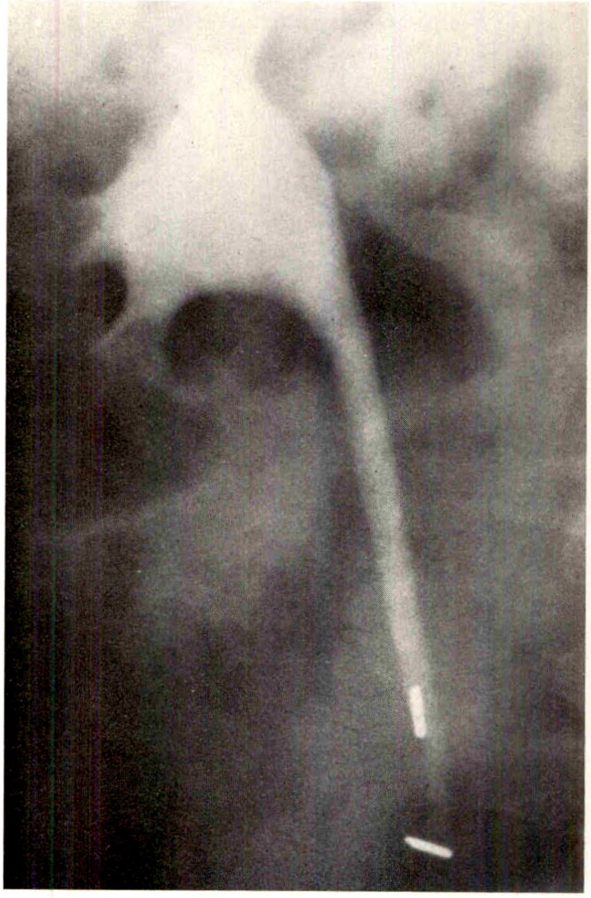

FIG. 3.

IVP examination one year later demonstrates the ureter is now smooth. Also the mild obstructive changes have now resolved.

1979, *British Journal of Radiology*, *52*, 504–506

REFERENCES

EKELUND, L., and LINDHOLD, T., 1974. Angiography in collagenous disease of the kidney. *Acta Radiologica Diagnosis*, *15*, 413–422.

FISHER, R. S., and HOWARD, H. H., 1968. Unusual ureterograms in a case of periarteritis nodosa. *Journal of Urology*, *60*, 398–404.

GLANZ, I., and GRUNEBAUM, M., 1976. Ureteral changes in polyarteritis nodosa as seen during excretory urography. *Journal of Urology*, *116*, 731–733.

PADOVANI, J., KASBARIAN, M., POLLINI, J., FAURE, F., and LEYNAUD, D., 1974. Interet de l'arteriographie renale dans la periarterite noueuse. *Annales de Radiologie*, *17*, 135–140.

SAMELLAS, W., BELLONIAS, E., and PAPACHARALAMPOUS, N., 1971. Polyarteritis nodosa: ureteral involvement. *Journal of Urology*, *105*, 186–187.

Bladder diverticulum: an uncommon cause of acute retention of urine in a male child

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(*Received October, 1978*)

Diverticula of the bladder in infants and children are mostly primary (congenital) rather than secondary to obstruction or neurogenic dysfunction (Boechat and Lebowitz, 1978). Although they are common only a few give rise to complications. One such complication is acute retention of urine (Williams and Eckstein, 1968), but it is rarely seen and very few cases have been illustrated in the literature. A case is presented to demonstrate this complication.

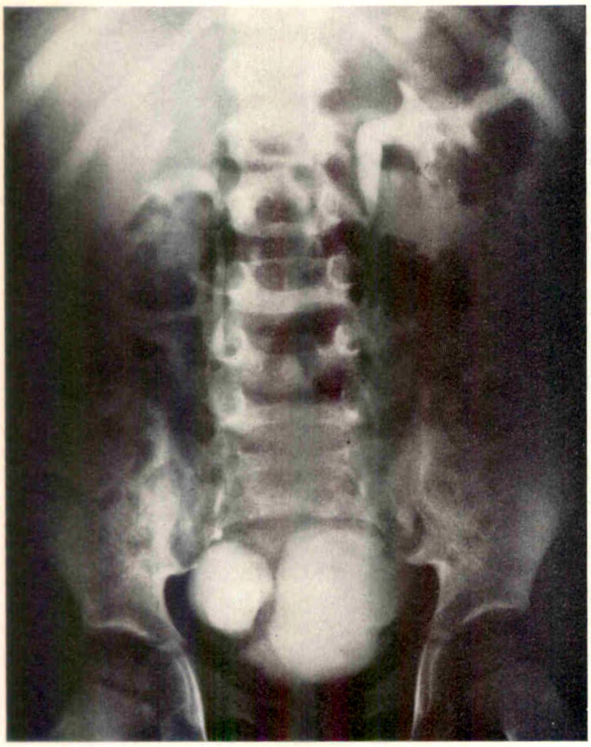

FIG. 1A.

IVU. Normal kidneys and unobstructed ureters. Two diverticula, one on each side of the bladder.

CASE HISTORY

A boy aged 3 years and 10 months was transferred to Birmingham Children's Hospital on April 13, 1977 for investigation and management of retention of urine. He had been admitted twice within six months to another hospital as an emergency with acute retention of urine and on both occasions he had catheter drainage of the bladder. On the first admission in November 1976 he was circumcized for a tight phimosis.

His parents said that he had had difficulty in passing urine since birth, *i.e.* straining, poor stream and dribbling associated with urgency and frequency, but very little urine

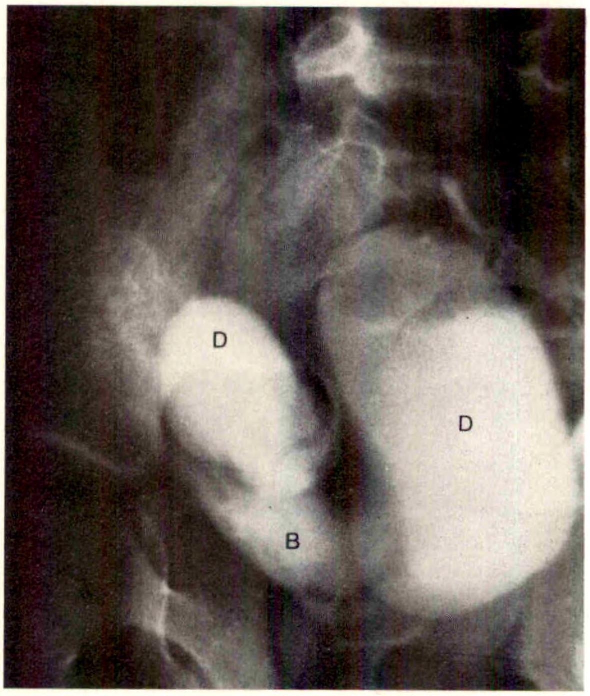

FIG. 1B.

IVU. Oblique view showing right ureter with a simple ureterocele-like dilatation at the ureteric orifice which opens into a right sided diverticulum. Large posteriorly positioned left diverticulum. B = Bladder. D = Diverticulum.

passed on micturition. This had persisted following the circumcision and urethral dilatation. In the past, according to the parents, he had had a few episodes of what one would describe clinically as sub-acute retention, but these did not require hospital admission as symptoms subsided overnight with bed rest and mild analgesics.

Excretory urography (IVU) showed unobstructed kidneys and ureters. The right single ureter had a simple ureterocele-like dilatation at the ureteric orifice which opened into a right sided bladder diverticulum (Fig. 1A and B). There was also another bladder diverticulum on the left.

Cystourethrography (CUG) confirmed the presence of postero-laterally situated and freely communicating diverticula, one on each side of the normal bladder. The left one had a larger capacity than the bladder. There was no vesico-ureteric reflux. On catheter withdrawal and initiation of micturition only a little contrast medium passed into the urethra, outlining normal anatomy (Fig. 2). Most of the contrast passed into the left diverticulum, causing its further distension and a descent downwards below the floor of the bladder, where it compressed the posterior urethra and produced a complete obstruction (Fig. 3). The patient was once again in acute retention for which he needed re-catheterization and drainage.

On cystoscopy (Mr. P. Gornall) urethra and bladder neck appeared normal. At laparotomy, the bladder had a thick wall and the ureteric orifice lay in the floor of each diverticulum. Bilateral diverticulectomy and re-implantation of the ureters were carried out. Follow up IVU and CUG examinations six months later showed satisfactory unobstructed appearances of the renal tract and a normal urethra.

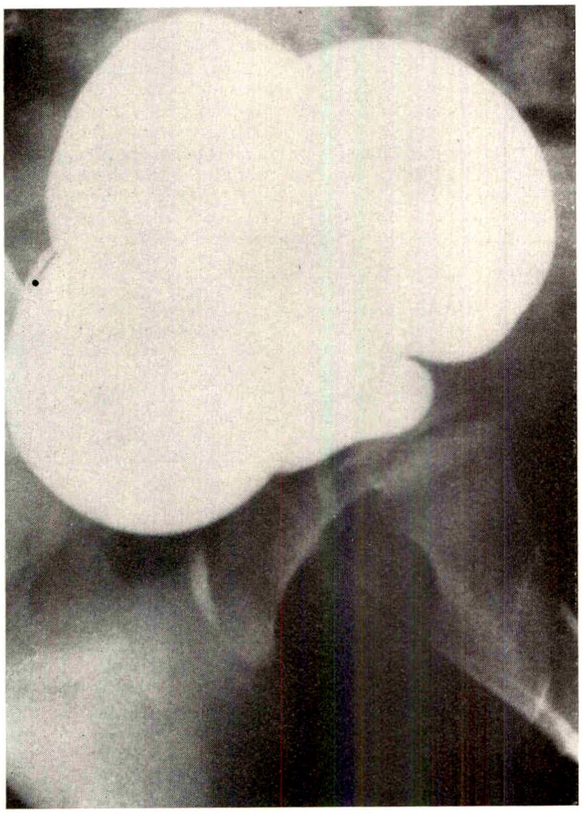

FIG. 2.

CUG. Initial phase of micturition showing normal position and anatomy of the unobstructed urethra.

DISCUSSION

Acute retention of urine in infancy and childhood is commonly due to urethral lesions such as posterior urethral valves, urethral diverticulum or distended ectopic ureterocele. Chronic retention of urine is usually associated with a neurogenic bladder in children with neurological disorders such as spina bifida and myelomeningocoele. Bladder diverticulum is one of the less common causes of acute retention.

In boys, spontaneous acute retention is more common than in adult life (Williams and Eckstein, 1968). This is likely to be due to the anatomy of the male urethra at this age; the posterior urethra is surrounded by immature prostatic tissue which is more easily stretched, and the bladder tends to be more of an abdominal organ. According to Williams and Eckstein (1968) if a diverticulum is present in the lower part of the bladder, as was the case in this patient, and becomes trapped in the pelvis, the

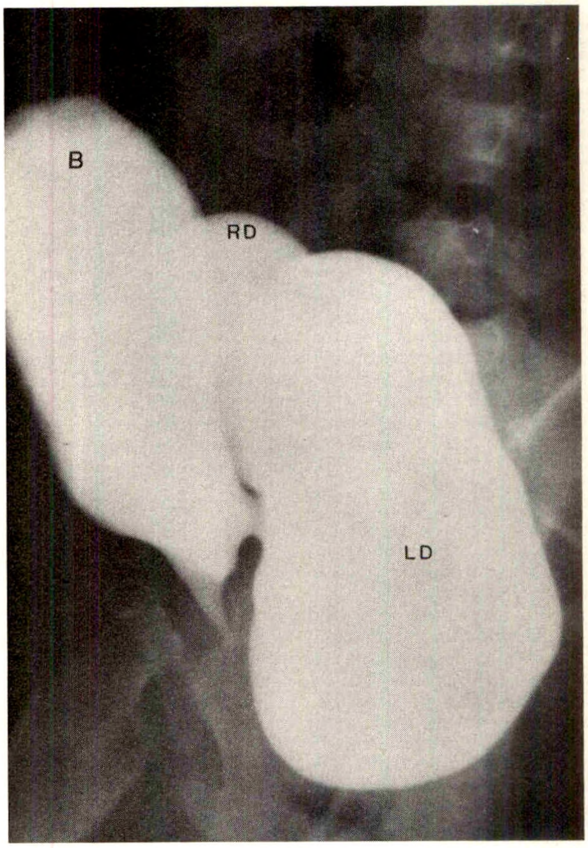

FIG. 3.

CUG. Later stage of the examination. Distended left sided diverticulum has descended downwards displacing the bladder forwards and upwards and stretching the posterior urethra resulting in a complete obstruction. B=Bladder. R.D.=Right diverticulum. L.D.=Left diverticulum.

bladder is further displaced upwards and the urethra stretched and compressed. In this case the contrast medium was seen to pass more readily into the diverticula than down the urethra, and as the left diverticulum enlarged and descended downwards, the urethra was seen to be more compressed and stretched leading to a complete obstruction and acute retention.

The history suggests that the patient had chronic retention. The intermittent acute episodes supervened when micturition was withheld for a long time and the diverticulum allowed to distend and descend to such a critical level as to cause a complete urethral obstruction.

Acknowledgment

At Birmingham Children's Hospital the patient was under the care of Mr. P. Gornall, F.R.C.S.

REFERENCES

Boechat, M. I., and Lebowitz, R. L., 1978. Diverticula of the bladder in children. *Paediatric Radiology*, 7, 22–28.

Williams, D. I., and Eckstein, H. B., 1968. Bladder disorders: diverticula. In *Paediatric Urology*, Ed. D. I. Williams, pp. 213–227 (Butterworth & Co., London).

Book review

Radiation Dose Limit for Embryo and Fetus in Occupationally Exposed Women NRCP Report No. 53, pp. 37, 1977 (*National Council on Radiation Protection and Measurements, Washington*) $3.50.

This report, together with its full supporting appendices, provides information on which to base a decision as to what dose to the fetus is acceptable for pregnant radiographers and technicians who wish to continue working. It also reviews the relationship between the staff member and her employer regarding the notification of pregnancy and the rights of both the mother and the fetus. The full review of present knowledge can also be applied to that other problem seldom referred to, as to the action to be advised when a patient has had radiological examination during early and unsuspected pregnancy.

The committee was appointed to review the basis for the existing NCRP recommendations that the maximum permissible dose equivalent to the embryo and fetus from occupational exposure of the expectant mother during the entire gestation period should be 0·5 rem, and to review the recently published information pertinent to this and to decide whether recent information warranted any change in the numerical limit.

In the event, the report confirms this level as being acceptable and states that there is no new evidence concerning teratogenic or carcinogenic effects of irradiation of the embryo-fetus that would justify a change in the limit in either direction.

Meticulous readers of ICRP 26 (and previously ICRP 9) will observe that the statement from NCRP of the maximum permissible dose to the embryo-fetus is somewhat more strict than that allowed under the ICRP. In the latest document it is possible for an embryo to receive 5 mSv (0·5 rem) during the first two months and the mother to receive not more than 9 m Sv during the remainder of the pregnancy. Hence by ICRP 26 the fetus is restricted to a dose of 14 mSv (1·4 rem).

The bulk of the remainder of the publication under review consists of a historical background and an excellent report on the status of knowledge in 1976 on aspects of the deleterious effect of irradiation of the embryo and fetus in humans and animals.

One of the problems in making accurate statements about probable risks is that when all the "ifs" and "buts" have been spelt out in full the non-mathematically and non-radiobiologically minded are immediately placed at a disadvantage. Perhaps the reviewer might this time be permitted to put his neck into the noose and suggest that, although the NCRP have quite correctly given all the facts in great detail, the picture for human data looks something like the following for risks to the fetus from radiation. This makes the assumption of course that the risk at the higher levels of dose may be extrapolated to doses of the order of one rad.

Radiation Risks	Risk per 1000 births from 10 mSv (1 rem)
Childhood leukaemia or malignancy in first 10 years of life (UNSCEAR 1977) (from X-ray doses about 0·20 rad)	0·2–0·25
Reduced head size using RBE of neutrons = 10 (from mixed γ and neutrons 28–57 rem)	1·7–2·5
Mental retardation using RBE of neutrons = 10 (from mixed γ and neutrons 140–280 rem)	0·14–0·29

R. E. Ellis.

1979, *British Journal of Radiology*, *52*, 507–508 JUNE 1979

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Carcinoma of cervix and HBO

THE EDITOR—SIR,

In a recent paper on hyperbaric oxygen and radiotherapy in advanced carcinoma of the cervix (Watson *et al.*, 1978), it was concluded that "a valuable improvement in local tumour control and in survival has been achieved with hyperbaric oxygen" and also that "a real improvement in the therapeutic ratio has been achieved . . .". The use of the terms "valuable improvement" and "real improvement" suggests that when such patients are being treated by irradiation this should be associated with the use of hyperbaric oxygen. However, in the same issue of the journal it was also stated, with reference to radiotherapy in hyperbaric oxygen for cervical carcinoma, that "when considering the overall results . . . we cannot draw any simple conclusion" (Dische, 1978).

Although the results reported by Watson *et al.* (1978) for stage III show increased local tumour control (71% HBO: 44% air) and survival (37%HBO: 25% air) at five years, the results obtained for treatment in air were poor. This was, in part, due to the regimes of treatment in air from two of the participating centres which produced results unacceptable by modern standards with local control in only 18% and 0% and survival of 8% and 0% respectively (Tables VI and XII, Watson *et al.*, 1978).

The data of Kottmeir for 19107 stage III patients from 118 institutions, treated between 1959 and 1963, show that 31% survived for five years (Marcial, 1977). Two other unrandomized but more recent series of patients treated in air have shown 36% (Cade and McEwen, 1978) and 42% (Joslin, 1978) survival at five years. In a randomized series of predominantly stage III, but advanced, patients treated at Leeds either in air or hyperbaric oxygen, local control was achieved in 69% and survival was 40% at five years and no advantage was found for treatment in hyperbaric oxygen (Ward and Dixon, 1979).

It seems that the results reported by Watson *et al.* (1978) for radiotherapy with hyperbaric oxygen for advanced carcinoma of the cervix were not better than those achievable by treatment in air either in this country or elsewhere (Glassburn *et al.*, 1974; 1977; Fletcher *et al.*, 1977; Bennett 1978). Taking generally available clinical data into account and also the reported increase of morbidity with hyperbaric oxygen (Fletcher *et al.*, 1977; Dische, 1978; Watson *et al.*, 1978), the time taken and the additional expense involved for treatment, it is our opinion that the use of the terms "valuable" and "real" is unjustified with respect to cervical carcinoma and should more properly be used only when the treatment in question is evaluated against results which are acceptable by current radiotherapeutic standards.

Yours, etc.,
A. J. WARD,
B. DIXON.

The Regional Radiotherapy Centre,
Cookridge Hospital,
Leeds LS16 6QB.

(*Received December 1978*)

REFERENCES

BENNETT, M. B., 1978. The treatment of stage III squamous carcinoma of the cervix in air and hyperbaric oxygen. Paper presented at British Institute of Radiology, Annual Congress, London, April 1977 (Abstract). *British Journal of Radiology*, *51*, 68.

CADE, T. E., and MCEWEN, J. B., 1978. Clinical trials of radiotherapy in hyperbaric oxygen at Portsmouth. *Clinical Radiology*, *29*, 333–338.

DISCHE, S., 1978. Hyperbaric oxygen: the Medical Research Council trials and their clinical significance. *British Journal of Radiology*, *51*, 888–894.

FLETCHER, G. H., LINDBERG, R. D., CADERUO, J. B., and WHARTON, J. T., 1977. Hyperbaric oxygen as a radiotherapeutic adjuvant in advanced cancer of the uterine cervix. Preliminary results of a randomized trial. *Cancer*, *39*, 617–623.

GLASSBURN, J. R., DAMSKER, J. I., BRADY, L. M., FAUST, D. S., ANTONIADES, J., PRASAVIN, CHAI, S., LEWIS, G. C., TORPIE, R. M., and ASBELL, S. O., 1974. Hyperbaric oxygen and radiation in the treatment of advanced cervical cancer. In *Fifth International Hyperbarix Oxygen Congress*, *II*, pp. 813–919 (Simon Fraser, University Vancouver).

GLASSBURN, J. R., BRADY, L. W., and PLENK, H. P., 1977. Hyperbarix oxygen in radiation therapy. *Cancer*, *39*, 751–765.

JOSLIN, C. A. F., 1978. The cathetron as part of the radical management of cervix cancer. In *High Dose-Rate After-Loading in the Treatment of Cancer of the Cervix*. Eds. Bates, T. and Berry, R., *British Journal of Radiology*, *Special Report 17* (in press).

MARCIAL, V. A., 1977. Carcinoma of the cervix. Present status and future. *Cancer*, *39*, 945–958.

WARD, A. J., and DIXON, B., 1979. Carcinoma of the cervix. Results of a HBO trial associated with the use of the cathetron. *Clinical Radiology* (in press).

WATSON, E. R., HALNAN, K. E., DISCHE, S., SAUNDERS, M. I., CADE, I. S., MCEWEN, J. B., WEIRNIK, G., PERRINS, D. J. D., and SUTHERLAND, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial in carcinoma of the cervix. *British Journal of Radiology*, *51*, 879–887.

Therapeutic ratio and radiosensitizers

THE EDITOR—SIR,

The recent results of the Medical Research Council Trials with hyperbaric oxygen (HBO) (Watson *et al.*, 1978; Dische, 1978) and the letter to the Editor (Hendry and Sutton, 1978), refer to the increase in normal tissue damage induced by HBO and misonidazole. It is unscientific and misleading to reduce the dose of irradiation by any given percentage when using such modalities.

The dose complication curve for normal tissue is sigmoid in shape. Thus the reported increase in severe complications from 3.8% (6/159) to 12.5% (20/161) using HBO cannot be considered equivalent to a 3% increase in irradiation dose unless we know where these points are on the dose complication curve for each tissue at risk. For example if one were to use the data available on lung tolerance following a single dose of whole-lung irradiation (Fryer *et al.*, 1978) such a change in incidence of complications would represent a dose enhancement factor (DEF) (defined as ratio of dose in air to dose in modified conditions to give an equivalent tissue effect) of 1.2 or a 20% difference in dose. The only safe way of calculating the DEF is to perform the type of studies described by Phillips and Fu (1978) in assessing the interaction of drugs and radiation in normal tissue. One can then determine whether there has been a true therapeutic gain, rather than merely an effective increase in radiation dose.

The overall local recurrence rate in IIB and III cancer of the cervix reported by Bush *et al.* (1978) was 31/135 which is less than in the hyperbaric oxygen group in the MRC trial. This suggests that a similar result might have been achieved by increasing the dose of irradiation. The data supplied by Hendry and Sutton on DEF is mainly confined to skin. Similar data for lung and gastro-intestinal tract should be generated before meaningful trials on sensitizers can be developed to answer this important question.

Yours, etc.,
C. J. H. Fryer.

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2656 Heather Street,
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British Columbia V5Z 3J3.
(*Received January 1979*)

REFERENCES

Bush, R. S., Jenkin, R. D. T., Allt, W. E. C., Beale, F. A., Bean, H., Dembo, A. J., and Pringle, J. F., 1978. Definitive evidence for hypoxic cells influencing cure in cancer therapy. *British Journal of Cancer*, *37*, *Suppl. III*, 302–306.

Dische, S., 1978. Hyperbaric oxygen: the Medical Research Council trials and their clinical significance. *British Journal of Radiology*, *51*, 888–894.

Fryer, C. J. H., Fitzpatrick, P. J., Rider, W. D., and Poon, P., 1978. Radiation pneumonitis: experience following a large single dose of radiation. *International Journal Radiation Oncology, Biology and Physics*, *4*, 931–936.

Hendry, J. H., and Sutton, M. L., 1978. Cure with radiosensitizer. *British Journal of Radiology*, *51*, 927–928.

Phillips, T. L., and Fu, K. K., 1978. The interaction of drug and radiation effects on normal tissues. *International Journal of Radiation Oncology, Biology and Physics*, *4*, 59–64.

Watson, E. R., Dische, S., Cade, I. S., Wiernik, G., and Sutherland, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial in carcinoma of the cervix. *British Journal of Radiology*, *51*, 879–887.

(*In reply*)

Hyperbaric oxygen

The Editor—Sir,

I am grateful to The Editors of The British Journal of Radiology for allowing me to see the letters written by Ward and Dixon and by Fryer (1979) prior to publication.

There is, in my view, no inconsistency between the report of a valuable or real improvement in the Medical Research Council trial in advanced carcinoma of cervix and the comment that we cannot draw any simple conclusion when all trials reporting treatment with hyperbaric oxygen and radiotherapy in carcinoma of the cervix are reviewed.

Although the treatment in air at two of the participating centres gave poor results, three-quarters of the cases were contributed by the other centres (Glasgow and Mount Vernon) where 20 and 27 fractions were employed. Taking these two centres together the improvement in local tumour control in those treated in oxygen compared with those in air for stage III disease was significant at the 0.001 level (calculation by Dr. Ian Sutherland).

A full examination of the data of Kottmeier will show that although 31% of all the 19107 stage III patients survived for five years there was a wide variation in results from institution to institution and from country to country. Even when comparing one series with another where the clinical stage and treatment are identical, wide variations in result are encountered. Many factors contribute to this including differences in the case material and differences in the application of criteria for staging. It serves no useful purpose to make such comparisons and especially to make them with series including a small number of patients or a different distribution of cases as to stage of disease.

The considerable benefit seen in the MRC study exists as a factual result. Watson *et al.* (1978), do not extrapolate the result beyond the context of the trial. It is unfortunately true that there is no such thing as a universally acceptable technique of radiotherapy for any site of tumour; however, that employed at Glasgow and Mount Vernon in the treatment of stage III carcinoma of cervix is not dissimilar from that used in many centres in the United Kingdom and I note that Ward and Dixon (1979) do not comment on this.

I entirely agree with Fryer (1979) as to the character of the dose-complication curve in normal tissues and that a 3% increment of radiation dose will result in a variable increase in morbidity according to the point at which we commence on the curve. There is, unfortunately, no way in which we can plot with precision the complication curve for human normal tissues. This is a difficult task to perform in laboratory animals and poses enormous practical and also ethical problems in man. We have, unfortunately, to make less satisfactory calculations when dealing with human data but comparisons of increment of morbidity with increment of benefit have real significance.

An increase in knowledge as to normal tissue effects and possible benefit with the use of sensitizing methods can only follow close collaboration in randomized controlled clinical trails. It is to be hoped that those who are critical of the results obtained in the MRC trials will be foremost among those taking part in new studies which will give even better data.

Yours etc.,
S. Dische.

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(*Received February 1979*)

REFERENCES

Fryer, C. J. H., 1979. Therapeutic ratio and radiosensitizers. *British Journal of Radiology*, *52*, 507–508.

Ward, A. J. and Dixon, B., 1979. Carcinoma of cervix and HBO. *British Journal of Radiology*, *52*, 507.

Watson, E. R., Halnan, K. E., Dische, S., Saunders, M. I., Cade, I. S., McEwan, J. B., Weirnik, G., Perrins, D. J. D., and Sutherland, I., 1978. Hyperbaric oxygen and radiotherapy: a Medical Research Council trial in carcinoma of the cervix. *British Journal of Radiology*, *51*, 879–887.

Background radiation and estimated risks from low-dose irradiation

The Editor—Sir,

In the analyses of cancer deaths among the Hanford workers by Mancuso *et al.* (1977) and Kneale *et al.* (1978) and in the various published discussions that have followed (Mole, 1978; Reissland and Dolphin, 1978; Kneale and Stewart, 1978; Sanders, 1978; Sagan, 1978; Reissland, 1978; Anderson, 1978, to name only some) two points have received less attention than seems warranted and one has not been considered at all. The first two points concern: (1) the lifetime radiation dose delivered by all sources and (2) the relationship of background radiation to observed cancer incidence and the deduction of a doubling dose; the third point is the extreme sensitivity of the "comparative mean dose" method (CMD) of calculating a doubling dose to errors in the dose estimation.

The mean life-time occupational doses received by the Hanford groups are small compared with those accumulated from natural radiation sources and possibly even from medical irradiation. By about the mean age of 60 years for the Hanford cases, the nominal background dose would be 6 rad. In the USA average bone marrow doses have been shown to range from 4.0 to 6.6 rad, depending on location (NRCP, 1975), and for an individual living in Richland, Washington State (nearest city to Hanford), the mean marrow dose is 5.2 ± 1.7 rad by age 60 years, though many individuals will have spent considerable periods in other parts of the country. Medical irradiation for diagnostic purposes is also far from negligible. Shlein *et al.* (1978) estimated that diagnostic radiology in the USA in 1970 resulted in a mean annual bone marrow dose of 103mrad per adult; the comparable figure for 1964 was 83mrad. It is probable, therefore, that Hanford workers could have received something like 10 rad to bone marrow by the age of 60 years, apart from doses received occupationally.

In testing any correlation between radiation dose and cancer, account must be taken of all relevant irradiation. The doses received by the Hanford workers were accumulated slowly over part or all of a lifetime. Because of the question of the latent period of cancer development it is not possible to specify an exact period over which the doses from the three sources should be added, but a maximum effective dose can be obtained by adding all the doses accumulated by any given age.

The second point refers to any method based on the concept of a dose that doubles the naturally observed rates of cancer as recorded in mortality statistics. Mancuso *et al.* (1977) state the linear response hypothesis in terms of a dose, D, that doubles the normal cancer death rate, A, assumed as "at zero dose". This level is derived, however, from mortality statistics that inevitably include the effect of some background-plus-medical dose, D_{NR}. We should therefore write:

$$A = A_0 + A_{NR} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where A_0 is the cancer risk attributable to causes such as heredity and all carcinogens except radiation and A_{NR} is the cancer risk that could be attributed to background and medical radiations. If the doubling dose, D, doubles the normal incidence, A, then a dose D_{NR} will produce a risk $A \,.\, D_{NR}/D$. Inserting this for A_{NR} in equation (1), and rearranging gives:

$$A_0 = A\,(1 - D_{NR}/D) \quad . \quad . \quad . \quad . \quad (2)$$

It follows that D cannot be less than D_{NR} without making A_0 negative. In other words, if the calculated doubling dose is equal to the background dose, then the latter must account for the total observed cancer incidence, a suggestion that would be contested by many geneticists. The value of the doubling dose for bone-marrow cancers is given by Kneale *et al.* (1978) as 3.6 rad, hence, if this were correct, background radiation alone should produce an incidence of these diseases twice as great as that actually observed. Kneale and Stewart (1978) have recognized this difficulty and suggest, wrongly in my view, that it points to inadequacies in the premises about the mode of action of radiation rather than to a fallaciously low doubling dose.

My third point is that doubling doses calculated by the CMD method are very sensitive to errors in dosimetry. Mancuso *et al.* (1977) effectively calculate the doubling doses from the formula:

$$D = (S - rR)/(r - R) \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where r and R are the mean doses respectively for the sub-population of cancer deaths and for the whole population and S is the mean squared dose for the whole population. From this it is clear that D depends on the ratio of two differences, both of which may carry considerable errors because the average doses, or products of doses, are derived from distributions that are very wide and also very skew. It also seems likely, from data available on radiation protection (UNSCEAR Report, 1977), that mean doses derived from measurements accumulated over long periods must carry errors at least of the order of $\pm 10\%$. Kneale *et al.* (1978) give the mean life-time occupational dose as 2.03 rad for all cancer deaths and 1.66 rad for the non-cancer deaths in the Hanford workers, while the value of S, the mean squared dose, is not stated. Hence in the denominator of equation (3) the difference in two mean doses that are as close as these must be subject to an error of the same order of magnitude as the difference itself and greater fractional errors may be expected in the numerator. Kneale *et al.* (1978) in fact give 95% confidence limits of 15.3 rad and 79.7 rad to the calculated doubling dose of 33.7 rad for all cancers, though it is not stated whether these include estimated errors in dosimetry.

Finally, any calculation of risk from low-dose occupational exposure requires, in addition to the occupational doses, a knowledge of the background and medical radiation doses received by the populations compared. In the more familiar "standardized mortality ratio" method the background and medical doses for the control population must also be determined, for they may not be the same as those for the occupationally exposed group, and the result depends both on differences in mortality and in dose. In the CMD method the requirement of accuracy in the doses is still more stringent, because differences in the squares and products of doses are involved. It hardly seems feasible that the necessary doses, occupational, background and medical, could be assembled with sufficient accuracy to support a calculation of risk retrospectively. If it could be done convincingly in a prospective study, it would be an enormous but valuable project.

Yours, etc.,
F. W. SPIERS.

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(*Received January 1979; revised February 1979*).

REFERENCES

ANDERSON, T. W., 1978. Radiation exposures of Hanford workers: a critique of the Mancuso, Stewart and Kneale report. *Health Physics*, *35*, 743–750.

KNEALE, G., STEWART, A., and MANCUSO, T. F., 1978. Re-analysis of data relating to the Hanford study of the cancer risks of radiation workers. In *IAEA International Symposium on Late Biological Effects of Ionizing Radiation*, Vienna, March, 1978.

KNEALE, G., and STEWART, A. M., 1978. Low-dose radiation. *Lancet*, *ii*, 262.

MANCUSO, T., STEWART, A., and KNEALE, G., 1977. Radiation exposures of Hanford workers dying from cancer and other causes. *Health Physics*, *33*, 369–385.

MOLE, R., 1978. Occupational exposure to ionizing radiation. *Lancet*, *i*, 1155.

NRCP, 1975. Natural background radiation in the United States. National Council on Radiation Protection and Measurements, Report No. 45, 69–74.

REISSLAND, J. A., and DOLPHIN, G. W., 1978. A review of the study of mortality among radiation workers at Hanford. *Atom*, *262*, 206–207.

REISSLAND, J. A., 1978. An assessment of the Mancuso study. National Radiological Protection Board Report No. NRPB–R79.

SAGAN, L. A., 1978. The Mancuso study: a comment. *Atom*, *262*, 207–209.

SANDERS, B. S., 1978. Low-level radiation and cancer deaths. *Health Physics*, *34*, 521–538.

SHLEIN, B., TUCKER, T. T., and JOHNSON, D. W., 1978. The mean active bone marrow dose to the adult population of the United States from diagnostic radiology. *Health Physics*, *34*, 587–601.

UNSCEAR, 1977. Sources and effects of ionizing radiations. United Nations Scientific Committee on the Effects of Atomic Radiation, 1977 Report, Annex E, 223–300.

1979, *British Journal of Radiology*, *52*, 510

Correspondence

The place of new contrast media in renal failure

The Editor—Sir,

We accept Dr. Golman's suggestion (1979) that our doubts about the value of dimers and non-ionic compounds as a means of improving the quality of the urogram in renal failure may be unnecessarily gloomy.

The point we wished to make was that in the experimental model we used to simulate renal failure neither of the new contrast media produced dramatic changes in urine iodine concentration. However, we would agree that in difficult clinical circumstances even a small increase in urine iodine concentration may be helpful. The question will only be resolved by a trial of the new agents in patients with renal failure.

We certainly agree with Dr. Golman that the lower osmolality of metrizamide is likely to be helpful in minimizing osmotic disequilibrium and reducing toxicity especially in patients with renal failure and in children.

Yours, etc.,
Judith A. W. Webb,
I. Kelsey Fry,
W. R. Cattell.

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West Smithfield,
London EC1A 7BE.

REFERENCE

Golman, K., 1979. Place of new contrast media in renal failure. *British Journal of Radiology*, *52*, 156.

Pharmacologically-controlled barium meal: a metoclopramide-glucagon sequential association

The Editor—Sir,

Metoclopramide (Primperan, Plasil b.n.) is very extensively used in this country in routine GI studies. The value of its speeding action is fully appreciated when modern fast-working radiological equipment is used. It saves time and unnecessary exposure. Glucagon is also by now an established drug, as an efficient and short-acting hypotonic agent.

During the past three years I have often found administration of the two drugs in sequence useful. This was done in a large number of routine studies and in 41 double-contrast studies.

In accordance with its more peripheral action, glucagon promptly stops previously induced metoclopramide hypermotility, producing full hypotonia and amotility. Performing tubeless duodenography one can readily get duodenal filling by metoclopramide, then by rapid glucagon i.v. injection, virtually freeze contrast progression at a suitable level, with little or no undesired opacification of the jejunum.

When using TV equipment, injection can be conveniently remote-controlled through double-length i.v. drip tubing. Moreover, in gastric work, I have often felt that previous parenteral metoclopramide made the stomach drier and so fitter for double-contrast studies.

Both drugs were used in the usual doses, *i.e.* 20 mg i.v. metoclopramide, 0.5–1 mg i.v. glucagon. Latency and duration of glucagon action were not noticeably modified. No untoward effect was observed. Patients have never reported the slight nausea sometimes associated with glucagon.

Yours, etc.,
A. Allufi.

Istituto di Radiologia Università Cattolica,
Rome, Italy.
(*Received December 1978*)

SI units in radiotherapy

The Editor—Sir,

I read with interest your continuing correspondence on the introduction of the gray and centigray into practical radiotherapy. I must, however, express concern at the comment made by Sandeman *et al.* (1979) when they write "Outputs of orthovoltage and superficial machines were given in terms of *seconds per gray*, as this retained reasonable sized numbers without going to submultiples and preserved the intentions of the SI system" (the italics are mine).

I should hope that the SI system is based on more scientific grounds than "reasonable sized numbers"; indeed, most opposition to SI is the unreasonableness of the numbers. But what are $s\ Gy^{-1}$? Your correspondents vaguely refer to output, which most readers, I believe, would interpret as dose rate at a standard distance, which by definition is measured in units of dose per unit time. Perhaps they mean inverse ontput?

The serious opponents to the gray are those worried by the ensuing confusion, but this surely is small in comparison to the use of inverse output. Let us preserve the intentions of SI and stick to physical concepts which are universally understood.

Yours, etc.,
C. K. Bomford.

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(*Received February 1979*)

REFERENCES

Sandeman, T. E., Millar, R. M., and Drummond, J. D., 1979. SI units in radiotherapy. *British Journal of Radiology*, *52*, 162–163.

X-ray vision

The Editor—Sir,

Recent correspondence initiated by Dr. Cochrane Shanks' account of the sensation of light experienced during a CAT scan recalls an article on vision by X rays by R. R. Newell (1948).

In 1953 I performed an experiment described in this article. Using a screening set operating at 3 mA and 80 kV and being well dark-adapted the sensation was of a very faint light of no definite colour. A metal pencil held in front of the eye produced, as expected, an image which was enlarged and inverted and moved in the opposite direction to the object. Some ten seconds sufficed and there is as yet no evidence of any harmful effect although I would not today repeat the experiment.

The wavelengths of the radiation involved are so different from those of the normal visible spectrum that the question arises as to whether the effect is due not to direct stimulation of the retina by X rays but to fluorescence within the structure of the eye.

Yours, etc.,
A. Bryce.

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(*Received February 1979*)

REFERENCES

Cochrane Shanks, S., 1978. CAT stimulation of retina. *British Journal of Radiology*, *51*, 837.

Newell, R. R., 1948. In *Modern Trends in Diagnostic Radiology* (First Series), ed. J. W. McLaren (Butterworth, London).

1979, *British Journal of Radiology*, *52*, 511

Correspondence

Appeal

THE EDITOR—SIR,

May I, through your correspondence columns, invite your readers to think for a moment of the information resources available to them?

British doctors have access to postgraduate medical centres, medical school, professional society and Royal College libraries, most of which have a bookstock in excess of 30000 volumes. Here in Papua New Guinea (PNG), our 10000 volume medical school library stands virtually alone serving not only the students but also the nation's medical, dental, paramedical and research personnel over a remote and inaccessible area three times the size of England and Wales. Many health workers live in isolated communities whose only contact with the capital is the airstrip and the radio-telephone. PNG has many health problems and there is much research to be undertaken. There is also a need to develop primary health care and health education projects, and to improve facilities for specialist training.

Famous in the medical world for rare diseases like kuru, PNG is not just a medical curiosity but a place where students, practitioners and researchers need a better information infrastructure. But our resources are too slender to be effective. We must improve our bookstock, extend the journals coverage and increase our audio-visual materials. On behalf of our present and future health care professionals, we seek your readers' assistance. Gifts of cash or kind suitable for medical and paramedical users would be very welcome.

Yours, etc.,
A. C. BUTLER.

University Library,
University P.O. Box 4819,
Port Moresby,
Papua New Guinea.
(*Received January 1979*).

Book reviews

Principles of Cardiovascular Nuclear Medicine. Edited by B. Leonard Holman, Edmund H. Sonnenblick and Michael Lesch. pp. vii+246, illust. 1977 (Grune & Stratton, New York, San Francisco & London) $18.50/£12·00.

The investigation of the cardiovascular system now occupies a large part of meetings devoted to nuclear medicine, and in this country an increasing amount of time is being spent in imaging the heart and investigating its performance by means of radionuclides. For anyone involved in this occupation this is the book—or the best available. Perhaps it is right to give it the title of "Principles" of Cardiovascular Nuclear Medicine since the practice changes with a rapidity which is liable to make any book out of date. All the chapters have previously appeared in print in "Progress in Cardiovascular Disease". They are all authoritative reviews by the leaders of this field of research and between them cover work up to 1976/77. This results in one very brief and incorrect mention of the use of krypton-81m (which is a pity), rather poorer pictures using thallium than one is now used to seeing displayed on view boxes and computers, and perhaps rather poorer tomographic images than are currently being produced. A chapter that is very worth keeping as a source of reference for anyone doing physiological work with tracers in the heart, is the one by James Basingthwaite who discusses the complex traps that lie in wait for the unwary enthusiast of "wash-out curves".

One aspect of contributions to nuclear medicine is the tendency for enthusiasm at the expense of scientific observation. For the most part this charge cannot be applied to the present volume and, in my view, it creates a valuable source of basic knowledge which will be useful even when the present techniques have been superseded.

J. P. LAVENDER.

Tactics and Strategy in Cancer Treatment. Recent results in cancer research. (series 62). Edited by Georges Mathé, pp. xv+219, illus. 1977 (Springer-Verlag, Berlin) DM.68.00/ $34.00.

The best way to indicate the scope of this book is to quote from the preface. "Tactics is the art of combining the action of all military forces with a view to victory. This work, which publishes the communications at the annual general meeting of the EORTC held in Paris in June 1976, was devoted to tactics and to the therapeutic strategy with a view to the recovery of cancer patients."

Under the heading of "Tactics" there are papers on human and animal work under the familiar headings of surgery, chemotherapy, immunotherapy and an additional section on monitoring. This includes biochemical aids to cancer management, laboratory tests for early diagnosis and the monitoring of progress.

The section on "General Strategy" opens with an introductory paper indicating the need for a strategic plan of management for cancer patients, in view of the multiple disciplines involved. In this section there are important contributions on the leukaemias and allied conditions, as well as multiple papers dealing with solid tumours. Among the contributors are many well-known names who have become leading authorities in their respective fields. The conclusions on the management strategy for various cancers are of considerable value to all clinicians engaged in oncology. Each contribution is accompanied by a full list of references.

This book provides an extremely useful summary of what is considered to be the present optimum treatment for many of the most common malignancies.

BRENDAN HALE.

1979, *British Journal of Radiology*, *52*, 512–520

Proceedings of the British Medical Ultrasound Society

Abstracts of papers presented at the tenth annual meeting of the British Medical Ultrasound Society held at The Civic Centre, Newcastle upon Tyne, on November 27–28, 1978.

The role of real-time scanning in obstetrics, by S. Campbell.
Comparison between a real-time linear-array scanner and a compound scanner for gestational aging by means of BPD measurements, by M. J. Bennett.
An anatomical biparietal diameter (The "sagittal" BPD), by G. B. Young, J. K. Williamson and R. W. Rawlings.
Ultrasonic visualization of fetal abnormalities, by D. Little, A. B. Roberts, A. Thoms and S. Campbell.
Ultrasonic screening for intra-uterine growth retardation, by J. P. Neilson.
A semi-automatic electronic planimeter for area and circumference measurement of ultrasound images, by. A. D. Christie and A. R. Rimmer.
Calibration problems encountered in area and circumference estimation from ultrasound scans, by M. F. Docker.
Clinical experience of cardiac visualization using a rotating transducer real-time ultrasonic scanner, by R. E. Scorgie, A. L. Muir, C. R. Bow, W. N. McDicken and T. Anderson.
Assessment of fetal and neonatal cardiac function by means of linear array multi-element and single beam transducers, by J. W. Wladimiroff, R. Vosters and W. Vletter.
The use of M-mode echocardiography to detect inco-ordinate left ventricular function, by R. Hall.
Diagnostic use of Doppler ultrasound in cardiology, by D. S. Tunstall Pedoe.
Doppler ultrasound in the evaluation of carotid artery stenosis—a comparative study, by M. Horrocks, V. C. Roberts and L. T. Cotton.
Doppler ultrasound in the detection of malignant tumours, by P. Atkinson, M. Halliwell, R. A. Mountford, A. J. Webb and P. N. T. Wells.
Doppler imaging of arterial grafts, by D. Bird, A. E. B. Giddings, R. Skidmore, J. P. Woodcock and R. N. Baird.
A Doppler vessel imaging system, by B. A. Coghlan.
Developments in ultrasound equipment, by N. A. Slark.
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Preliminary measurements of attenuation of ultrasound in placental tissue, by M. Kearle and M. F. Docker.
The value of real time ultrasound in abdominal diagnosis, by H. B. Meire and Pat Farrant.
The significance of ultrasonic gallbladder wall thickening, by R. C. Sanders and E. Zerhouni.
Grey-scale ultrasonography and endoscopic pancreatography in pancreatic diagnosis, by W. R. Lees.
The ultrasonic demonstration of human follicular and corpus luteum development: a new method for observation of ovarian development, by B.-J. Hackeloer.
Carcinoma of the ovary—correlation of ultrasound and X-ray computed tomography with second look laparotomy, by S. J. Pussell, D. O. Cosgrove, E. Wiltshaw, J. Hinton, G. H. Barker and Janet E. Husband.
Radial scans of the extrahepatic biliary system in obstructive jaundice, by J. G. Duncan.
A prospective study of thyroid ultrasonography, by W. R. Lees, L. R. Watson and R. C. G. Russell.

THE ROLE OF REAL-TIME SCANNING IN OBSTETRICS

By S. Campbell

King's College Hospital, London

Because of the rapid improvement in the quality of images from real-time scanners over the past two years, many of the obstetric investigations previously undertaken by static B-scanning can now be adequately covered and more rapidly performed by real-time scanning techniques. In addition, studies of fetal behaviour and activity can now be made which add a new parameter to the evaluation of fetal well-being. The potential role for real-time scanning and the type of real-time scanner most suited for the many different investigative techniques were discussed.

COMPARISON BETWEEN A REAL-TIME LINEAR-ARRAY SCANNER AND A COMPOUND SCANNER FOR GESTATIONAL AGING BY MEANS OF BPD MEASUREMENTS

By M. J. Bennett

Queen Charlotte's Maternity Hospital, London

A random sample of 350 ante-natal patients was scanned by separate individuals each using one of the machines. Each patient was examined on the same day and neither individual was aware of the others' findings. The range of gestational ages was 14–40 weeks.

The results showed that the real-time system was able to obtain clinically useful readings in the majority of cases. The mean BPD reading obtained with this system was 0.29 mm more than that obtained with the compound scanner. It was found however that whereas 1% of fetal heads were in such a position that an acceptable BPD could not be obtained with the compound scanner, 14% of fetal heads could not be adequately measured with the linear array system. These failures not only occurred during the third trimester, and are a result of the transducer size, but are also an indication of how careful an operator has to be about what measurements to accept.

AN ANATOMICAL BIPARIETAL DIAMETER (THE "SAGITTAL" BPD)

By G. B. Young, J. K. Williamson and R. W. Rawings

Department of Radiodiagnosis,
Simpson Memorial Maternity Pavilion and
The Royal Infirmary, Edinburgh

As observed by McDicken (1976), the biparietal measurement "started as a simple A-scan technique, then developed to use both A- and B-scan and will doubtless improve further, particularly as the ultrasonic images (of the contents of the fetal skull) become more detailed."

It has seemed to the authors for some time that these additional details are now available and that it is possible to construct a recognizable and consistent anatomical pattern of the brain at or near the maximum biparietal diameter. The anatomical BPD we have found most useful lies in a transverse plane and is arrow-shaped. The shaft of the arrow, however, lies also in the sagittal plane, and bearing in mind the derivation of sagittal (L. sagitta—an arrow), this biplane pattern may be aptly referred to as the "sagittal" biparietal diameter.

The arrow points to the occiput of the fetal skull and it would seem that it is produced by the sloping walls of the cisterna vena magna or quadrageminal cistern, which lies at and just below the tentorium and possibly a portion of the posterior lateral walls of the right and left ambiens cisterns as they sweep round the brain stem. The midline itself from the arrow tip forwards consists of the meningeal coverings of the great vein of Galen, the midline structures in the region of the pineal gland, the third ventricle, the septum lucidum between the foramina of Munro, and the falx, in that order.

There are four additional pieces of evidence to support this anatomical localization of the arrowed midline pattern. The pattern is shown in illustrations in a paper by Kossoff *et al.* (1974). On CAT scans the pattern is admirably depicted when the sections are taken at 20 deg to the anthropological base line. At the more conventional 30 deg angle, the arrow point is blunted and its curved edge represents the free edge of the tentorium itself. Third, we have observed on the A-scan in sectional scanners, and also clearly on real-time machines, two pairs of strong arterial pulsations lateral to the tips of the barbs of the arrow. The most medial pair are usually stronger and presumably represent pulsations in the right and left posterior cerebral arteries. The more peripheral pulsations are thought to be formed by the vessels of the choroid plexus as they sweep downwards and forwards along the floor of the temporal horns of the lateral ventricles. Fourthly, the anatomy can be demonstrated in layers sterioscopically on the Sonicaid multiplanar scanner.

Measurements of the biparietal diameter using both the conventional method first described by Campbell (1968) and the "sagittal" BPD are currently being recorded and analysis of the first sixty measurements shows agreement between the two methods to within 0.25 mm with an average difference of 0.08 mm.

The "sagittal" BPD or arrowed midline is presented as a practical alternative to the conventional biparietal diameter. As it is a standard and recognizable pattern it is consistent when repeated, and therefore ideal for sequential measurements required for assessment of fetal growth. In fetal age estimation, it would seem so near the established norm that it is also of practical value.

In BPD estimations by real-time the observation of the arrow and the arterial pulsations greatly assist location of the correct lateral angle and the measurement of a technically competent BPD. In addition, when the "sagittal" BPD is used, the fetal lie is clearly established as there can be no doubt as to the position of the fetal occiput. The heart beat is identified without searching for it in the fetal chest, and finally any degree of hydrocephalous is automatically identified or excluded.

REFERENCES

CAMPBELL, S., 1968. An improved method of fetal cephalometry by ultrasound. *Journal of Obstetrics & Gynaecology of the British Commonwealth*, *75*, 568–576.

KOSSOFF, G., GARRETT, W. J., RADAVANOVICH, G., 1974. Ultrasonic atlas of normal brain of infant. *Ultrasound in Medicine & Biology*, *1*, 259–266.

MCDICKEN, W. N., 1976. *Diagnostic Ultrasound* (Crosby Lockwood Staples), p. 156.

ULTRASONIC VISUALIZATION OF FETAL ABNORMALITIES

By D. Little, A. B. Roberts, A. Thoms and S. Campbell

King's College Hospital, London

In women with raised amniotic fluid or maternal serum alphafeto-protein levels (AF-AFP & MS-AFP respectively) ultrasound examination confirms the presence of a lesion in over 90% of cases.

Several sacral spina bifidas and a small occipital myelocele have been missed. Fetuses with omphaloceles have a high incidence of serious associated anomalies. However, the parents of a fetus with a minor abdominal wall defect may wish to continue the pregnancy.

Ultrasound contributes to the management of difficult cases, *i.e.* those with (i) borderline AF-AFP levels (three to seven standard deviations above the mean); (ii) when amniocentesis is declined due to fear of an abortion; (iii) amniocentesis sample contaminated with fetal blood and (iv) late presentation (after 20 weeks gestational age).

We have now seen five cases with borderline AF-AFP levels in which ultrasound correctly predicted a normal fetus. One patient underwent a termination in another unit on the basis of the AF-AFP alone. In a further case an omphalocele was missed, but this was before a detailed examination of the umbilical cord insertion was performed routinely in such cases. Analysis of the number and morphology of rapidly adhering cells in the amniotic fluid and real-time ultrasound guided fetoscopy has been helpful in these pregnancies.

A number of other abnormalities have been recognized before 24 weeks gestational age, *i.e.* in time for termination of pregnancy to be offered. In the majority of these patients AF-AFP was normal.

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ULTRASONIC SCREENING FOR INTRA-UTERINE GROWTH RETARDATION

By J. P. Neilson

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The ante-natal clinical detection rate of the "small for dates" fetus is reported as less than 40%. As a group, these fetuses have a higher incidence of perinatal mortality and morbidity, and, in the long term, a higher incidence of neurological and intellectual impairment, when compared with infants of a birth weight appropriate for gestational age. Therefore, the ante-natal detection of the "small for dates" fetus is desirable to permit careful monitoring and delivery at the optimal time, under the optimal circumstances. Preliminary findings are presented of the efficacy of screening the pregnant population, at between 34 and 36 weeks of gestation, utilizing seven ultrasonically-measured fetal parameters, to detect those fetuses whose birth weight will be below the fifth centile for the population. The fetal parameters measured were crown-rump length, biparietal diameter, head area, head circumference, trunk area, trunk circumference and transverse trunk diameter.

A SEMI-AUTOMATIC ELECTRONIC PLANIMETER FOR AREA AND CIRCUMFERENCE MEASUREMENT OF ULTRASOUND IMAGES

By A. D. Christie and A. R. Rimmer

Ninewells Hospital, Dundee

Recent developments in fetal growth monitoring have extended to area and/or circumference measurements of fetal head and trunk sections in addition to the simpler measurement of the biparietal diameter which is now known to be of limited value on its own. Most circumferences and areas are measured from a photographic recording of the relevant areas by means of a manually manipulated map measurer or planimeter. We have devised a new means of obtaining the results required using the parameters and caliper system already available in most B-scanning systems. Our system has been fitted to the Nuclear Enterprises "Diasonograph" 4102B.

The basic principle of the instrument uses the electronic caliper to make a series of measurement of the "radii" of the image to be examined at regular increments. The calculation of the area then reduces to finding the average of the "radii" squared, and multiplying by a constant.

Modern pocket calculators are very inexpensive and versatile. We use two of these to perform the two functions required. For measurements of area we use the following programme: enter radius, —square—memory plus—memory recall.

For circumference we use: enter radius—memory plus—memory recall. At the end of the final sequence the operator keys into each calculator the appropriate multiplier and receives the answer.

In order to maintain accuracy and to interfere with the existing apparatus as little as possible, the sine/cosine potentiometer and the X and Y positional potentiometers are switched out, and an identical duplicate set switched in. The new X and Y potentiometers are used to position the scanning beam relative to the area to be measured which has been stored on the storage oscilliscope display. The new sine/cosine potentiometer is driven through 360 deg by an electric motor with positional pulses generated every 7.5 deg. The motor always starts in the same position and can be stopped at any point. With the proximal caliper spot situated as near to the centre of the area as possible, the distal caliper spot is steered by the operator, around the periphery of the area, using the distal caliper control. The speed of rotation is 60 sec for one revolution, assuming no stopping. The readings are fed to the calculators automatically every 7.5 deg of rotation. The calculators are relatively slow and for the worst case take just less than 0.9 sec for one program. We therefore have a compromise involving accuracy of measurement, speed of measurement and calculator speed.

Examples were given of clinical applications.

CALIBRATION PROBLEMS ENCOUNTERED IN AREA AND CIRCUMFERENCE ESTIMATIONS FROM ULTRASOUND SCANS

By. M. F. Docker

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Measurement of biparietal diameter of the fetus is essentially a measurement of transit time of an ultrasonic pulse, and equipment can readily be calibrated for this parameter. Circumference and area measurement call for a greater degree of display calibration, especially in the case of real time systems. This paper attempted to point out some of the pitfalls to be encountered.

CLINICAL EXPERIENCE OF CARDIAC VISUALIZATION USING A ROTATING TRANSDUCER REAL-TIME ULTRASONIC SCANNER

By R. E. Scorgie, A. L. Muir, C. R. Bow,
W. N. McDicken and T. Anderson

Royal Infirmary, Edinburgh

We have previously described a mechanical real-time ultrasonic sector scanner which is based on a rotating transducer principle (Bow *et al.*, 1979). We have now used this device to examine 50 patients suffering from a wide variety of cardio-respiratory diseases. Using a left parasternal approach, cardiac-visualization was good in most patients, but in some a subxiphoid approach gave the best results. Mitral and aortic valves and the left ventricle were nearly always well seen and regional wall movement could be assessed. Segmental abnormalities of left ventricular wall motion corresponded well with abnormalities demonstrated by isotope angiography. The device gives good cardiac visualization and its small transducer head size readily allows subxiphoid examination.

REFERENCE

BOW, C. R., MCDICKEN, W. N., ANDERSON, T., SCORGIE, R. E., and MUIR, A. L., 1979. A rotating transducer real-time scanner for ultrasonic examination of the heart and abdomen. *British Journal of Radiology, 52*, 29–33.

ASSESSMENT OF FETAL AND NEONATAL CARDIAC FUNCTION BY MEANS OF LINEAR ARRAY MULTI-ELEMENT AND SINGLE BEAM TRANSDUCERS

By J. W. Wladimiroff, R. Vosters and W. Vletter

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Serial ultrasonic studies of fetal and neonatal cardiac function were performed in 11 patients between 36 and 42 weeks of gestation.

Fetal scan. First, the position of the AP diameter of the fetal chest at the level of the heart was identified on a cross-section, using two-dimensional real-time ultrasound. The next step was the positioning of a single beam transducer at an angle of 45 deg to the AP chest diameter, in order to produce an echocardiogram (T-M mode) of the left ventricle (LV) right ventricle (RV) and interventricular septum (IVS). Simultaneous fetal ECG's were made using scalp clip-electrodes.

Neonatal Scan. Here, the first step in identifying the position of the AP diameter was omitted. The remainder of the procedure was as described in the fetal scan. Simultaneous neonatal ECG's were made.

In each patient an echocardiogram and electrocardiogram was made of the fetus during the first stage of labour, and of the neonate within 10 minutes, 4 hours, 1 day and 2 days following delivery. In the 11 fetuses, RV (end-diastolic) diameter varied from 13.8–19.6 mm. LV (end-diastolic) diameter varied from 13.7–18.8 mm. Left to right ventricle ratio varied from 0.92–1.05. Right ventricular ejection time ranged from 172 to 202 msec; left ventricular ejection time ranged from 174 to 201 msec. Fetal heart varied from 125 to 150 b.p.m.

The pattern of fetal interventricular septal movement varied substantially amongst the patients studied. Patterns from normal to paradoxical were observed.

Immediately after delivery, an increase in ventricular left-to-right ratio was observed. This increase varied from 62.5–112%. The left and right ventricular ejection times varied from 170–220 msec. Patterns of interventricular septal movement in the neonatal period were normal. Finally, computer analysed data of fetal and neonatal tracings were given of change in LV and RV dimension during several consecutive heart beats, *i.e.* values of mean peak positive and peak negative velocity. Fractional shortening (FS) of LV and RV dimension, *i.e.* the total shortening of the echographic LV or RV dimension expressed as a proportion of the end-diastolic dimension or percentage change in dimension during systole. $\mathrm{FS}\ (\%)=(\mathrm{DD}-\mathrm{SD})/\mathrm{DD}\times 100$. DD and SD are end-diastolic and end-systolic LV or RV dimensions.

THE USE OF M-MODE ECHOCARDIOGRAPHY TO DETECT INCO-ORDINATE LEFT VENTRICULAR FUNCTION

By R. Hall

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In the past M-mode echocardiography was thought to be unsuitable for the assessment of left ventricular function in ischaemic heart disease since the echo beam examined only a small area of the left ventricle and, characteristically, ventricular damage is patchy in ischaemic heart disease. Recently the use of simultaneously recorded apex and echocardiograms has allowed an accurate assessment to be made of this inco-ordinate left ventricular function in ischaemic heart disease.

DIAGNOSTIC USE OF DOPPLER ULTRASOUND IN CARDIOLOGY

By D. S. Tunstall Pedoe

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Blood flow velocity and direction within the heart and great vessels demonstrated by transcutaneous Doppler ultrasound can give useful indications of disordered haemodynamics and is complementary to the anatomical information given by echocardiography in the diagnosis of heart disease.

Measurements have been made with a Sonicaid BV 380 8 MHz continuous wave Doppler instrument from the subclavian arteries and internal jugular vein, and with a SINTEF-PEDOF 2 MHz range gated and continuous wave Doppler instrument for intrathoracic blood velocities.

Cardiac valvular stenoses have been demonstrated by locating the jet and measuring the abnormally high transvalvular blood velocity or by demonstrating turbulent vortices convected downstream from the jet.

Cardiac valvular regurgitation can be demonstrated by showing inappropriate reversal of flow. For example in mitral regurgitation a systolic jet >4 metres/sec can be shown passing from the left ventricle to the left atrium. This jet can be tracked with range-gated Doppler but to measure its velocity continuous wave Doppler with either a very sensitive maximum frequency estimator or sound spectrograph has to be used.

Directional spectrographs are of particular value. In mixed mitral valve disease, with the Doppler probe aligned with the mitral valve, a systolic high velocity jet going away from the probe back into the left atrium and indicating mitral regurgitation, is followed by a diastolic jet coming towards the probe, the maximum velocity of which is a direct indication of the pressure drop across the mitral valve and thus of the severity of the mitral stenosis.

The effects of dysrhythmias, drugs and exercise can be demonstrated by this non-invasive technique.

This work is supported by the British Heart Foundation.

DOPPLER ULTRASOUND IN THE EVALUATION OF CAROTID ARTERY STENOSIS—A COMPARATIVE STUDY

By M. Horrocks, V. C. Roberts and L. T. Cotton

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A prospective study has been undertaken on 22 patients with varying degrees of carotid artery stenosis, to establish the relationship between the degree of internal carotid artery stenosis as estimated by arteriography, and three non-invasive techniques, all using continuous wave Doppler velocimetry.

The first technique is measurement of the pulse wave transit time in the internal carotid artery, and normalizing this by dividing it by the shortest of either the frontal or brachial transit times to produce a transit time ratio. This technique was able to differentiate between 0–20% stenosis, 21–50% stenosis and >50% stenosis ($p=0.001$).

The second technique involved taking sonograms of the common carotid and supra-orbital arteries, and comparing the height of the first peak (A) to the second peak (B) to produce a ratio—the A/B ratio. On comparing the three groups of carotid stenosis, we were unable to find any statistical difference.

The third technique is the temporal artery occlusion test (TAOT) which we found to be unreliable in diagnosing carotid artery stenosis of $> 50\%$.

In conclusion the transit time ratio was the most useful investigation and the accuracy was not increased by adding the other two techniques.

DOPPLER ULTRASOUND IN THE DETECTION OF MALIGNANT TUMOURS

By P. Atkinson, M. Halliwell, R. A. Mountford, A. J. Webb and P. N. T. Wells

Bristol General Hospital

A commercially available 10 MHz Doppler flowmeter has been used to examine malignant tumours lying in the superficial soft tissues. These include breast carcinomas and lymph nodes involved with chronic lymphatic leukaemia, lymphoma and metastatic carcinoma. Doppler signals have been detected arising from these tissues presumably related to their increased vascular supply. Arterial and venous signals have been detected, thought to represent new supply vessels. In addition a minority of neoplasms give rise to a "characteristic" signal, possibly due to arterio-venous shunting.

This paper presented the results of Doppler studies on 200 patients presenting with lumps in the breast, and on 50 patients with various types of malignant lymphadenopathy. The way in which the Doppler signals seem to change in response to radiotherapy or combination chemotherapy was also discussed.

DOPPLER IMAGING OF ARTERIAL GRAFTS

By D. Bird, A. E. B. Giddings, R. Skidmore, J. P. Woodcock and R. N. Baird

Bristol Royal Infirmary

Successful limb salvage can be achieved by dacron grafts inserted distal to the inguinal ligament, but the long term patency rates are not good. The factors which lead to graft occlusion are poorly understood but stenosis due to layering of fibrin and fibrous connective tissue on the internal surface of the graft has been recognized as an important contributory factor, and early detection and correction of stenosis in arterial grafts can prevent graft failure. This study was performed to evaluate a new non-invasive vessel imaging technique and its application to the study of arterial grafts.

A 5 MHz multichannel pulsed Doppler artery and vein imaging system (MAVIS, GEC Medical) was used to perform 128 scans in 60 limbs following surgery for arterial disease of the leg. 25 long dacron grafts (18 iliopopliteal; 7 axillofemoral) and 14 short proximally inserted dacron grafts (10 aortofemoral; 4 iliofemoral) were studied. Transverse sections and lateral scans were performed at each site.

Comparability of transverse and lateral scans was good, 24 paired scans giving virtually identical internal diameters (ID 8.46 ± 0.36 mm; 8.67 ± 0.36 mm; mean $\pm$ SEM, difference NS).

Eighteen iliopopliteal grafts (10 mm ID) scanned at three sites (inguinal, midthigh, popliteal) showed no decrease in internal diameter from the inguinal site to midthigh (7.62 ± 0.35 mm to 7.84 ± 0.36 mm, difference NS) but there was a significant decrease in graft lumen from midthigh to popliteal level (7.84 ± 0.36 mm to 6.31 ± 0.44 mm; $P < 0.01$).

There was no evidence of distal graft stenosis in the 14 shorter grafts studied (mean ID 10.24 ± 0.50 mm) but marked enlargement was detected at three femoral anastomoses suggesting aneurysmal dilatation.

In three grafts localized stenoses were detected, including stenosis of the suprapubic limb of one axillobifemoral graft which was subsequently confirmed at autopsy. Narrowing of the distal segments of two axillofemoral grafts was also noted.

These results show that this imaging technique gives reproducible results and can detect changes in graft lumen. Narrowing of the lumen distally in iliopopliteal dacron grafts has been shown, and it is suggested that failure of these long grafts may be due to distal graft stenosis which was not detected in shorter grafts.

A DOPPLER VESSEL IMAGING SYSTEM

By B. A. Coghlan

Guy's Hospital Medical School, London

Continuous-wave Doppler flowmeters are now used to produce two dimensional vessel images. We have constructed a scanner incorporating audio spectral analysis, raster-scan display and data storage under micro-processor control. Software allows the use of a high level language (BASIC).

This has made possible the production of vessel images using various criteria to study ways of improving image quality. It has also been possible to post-process the images obtained to enhance quality.

The system was outlined, and the various techniques of image processing described and results shown.

DEVELOPMENTS IN ULTRASOUND EQUIPMENT

By N. A. Slark

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In recent years the annual meeting of the American Institute for Ultrasound in Medicine (AIUM) has offered a regular opportunity to assess the current state of development of ultrasound diagnostic instrumentation, based on both the large and comprehensive technical exhibition and also on the papers presented.

This paper attempted to present a current assessment of trends in instrumentation, based on the 1978 AIUM meeting held in San Diego in October 1978. In addition some particularly novel or especially important B-scan instruments were discussed in more detail and brief references were made to other areas of interest to users of ultrasound, *e.g.* tissue characterization.

PLEASE NOTE: As in previous years the Scientific and Technical Branch of DHSS will publish a report covering the AIUM meeting from the equipment point of view. Copies of the report on the San Diego meeting may be obtained, free of charge, by writing to Mrs. A. Noble, Room 423, 14 Russell Square, London WC1B 5EP.

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THE DEVELOPMENT AND APPLICATION OF CONTACT SCANNING EQUIPMENT FOR THE ULTRASONIC EXAMINATION OF THE GLOBE AND ORBIT

By G. V. Catford, H. W. Taylor and R. Targett

St. George's Hospital, London

The paper described two equipments which have been developed for the ultrasonic examination of the globe and orbit.

The first provides an automatic sector scan from the required test point on the lid. The second is manually operated and provides a compound scan around the required arc on the lid. Both equipments are mounted on a low pressure air bearing plate which enables the clinician to position the transducer easily and precisely on the patient's lid. These equipments have proved very acceptable to the patients in routine use.

The paper discussed briefly the advantages and disadvantages of contact scanning via the lid. It gave examples of the results obtained and discussed their clinical interpretation.

This programme of work was supported by the DHSS and Messrs. Nuclear Enterprises.

ORTHOGRAPHIC TRANSMISSION IMAGING—RECENT RESULTS WITH THE SRI ULTRASONIC CAMERA

By P. S. Green, W. F. Mullen, J. F. Holzemer and J. R. Suarez

SRI International, Menlo Park, California, USA

The attractiveness of real-time orthographic, transmission imaging lies, in part, in its image presentation, which is similar to that of fluoroscopy. For some applications this perspective view is more readily interpreted than the cross-sectional B-scan.

To realize the potential of orthographic imaging, SRI International has developed, and continues to improve, its ultrasonic camera. The camera incorporates two ultrasonic lenses which form a focused image field, two counter-rotating prisms to scan the image field past a linear array composed of 192 receiving elements and the necessary electronics to produce a television image. A digital scan converter was developed recently and installed in the system.

Also recently developed is a diffuse insonification system that eliminates diffraction artifacts, producing images that more faithfully depict the attenuation differences in tissue. The images now appear more like those obtained by radiographic techniques.

A variety of clinical applications for orthographic transmission imaging is now emerging. In orthopaedics, visualization in real-time of the extremities, the shoulder and the hip demonstrates dynamically the interaction of muscle, cartilage, bone, tendon and joints. Application to the newborn could permit rapid and accurate determination of congenital hip displacement. The superficial blood vessels in the extremities are often displayed with striking clarity.

In the abdomen, the kidneys, liver and other organs can be visualized; respiratory motion aids in their identification and delineation. The narrow depth-of-focus minimizes the effects of out-of-focus tissues in those of interest. For example, the viewer may first focus on the rib cage, observe its bony and cartilaginous portions as well as the associated musculature, then focus on deeper organs without interference from the out-of-focus ribs. Much of the gastrointestinal tract is usually visualized, especially those portions that are gas filled. Haustral patterns in the colon are well delineated and peristalsis in the small intestine may be observed. Other applications including visualization of the breast have also been explored with encouraging results.

A film was presented that illustrated the operating principles of the camera and included images demonstrating the uses described above.

This research was supported by Grant GM-18780 from the National Institutes of General Medical Sciences.

AN IMPROVED PROBE FOR THERAPY OF MENIERE'S DISEASE

By T. A. Whittingham, M. J. Farmery and I. Frew

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Treatment of Meniere's disease by ultrasonic irradiation of the semi-circular canal has been performed on approximately ten patients per year for the last 15 years at Newcastle General Hospital. Until recently commercial apparatus, manufactured by Elliot, has been used.

This presentation described the design of a new "slimline" probe for use with this apparatus. The important features of the new design are: (i) a nozzle diameter of 3 mm, compared with 6 mm in the original; (ii) a temperature sensor built into the probe itself.

Benefits arising from the new design are as follows:

1. A smaller mastoid cavity is now required with subsequent alleviation of patient trauma and operating time.
2. The surgeon's view of the probe tip is improved.
3. The temperature at the probe tip is reliably and repeatably monitored.

ULTRASONIC DOSIMETER MARK II

J. Szilard

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When treating a patient with ultrasound it is important to ensure that he receives the actual dosage prescribed by the doctor. However, coupling between applicator and patient may vary. Also diagnostic devices must not exceed a safe dosage.

A simple method has been devised to solve the above problem by introducing an ultrasonic power measuring bridge between the applicator head and the patient.

A thermocouple or a thermistor surrounded by an absorbant bead of plastic or wax etc. will show, when irradiated, a temperature rise due to the energy directly absorbed by the bead and due to the friction induced by the ultrasound between the bead and thermocouple or thermistor. This is a well-known method for measuring intensity omnidirectionally.

Two sets of thermistor beads embedded in a plate, shielded on one side by a tiny blob of porous material, are fed from a constant current source. By taking the difference of the voltage drop across them the ultrasonic power passing through the plate may be measured.

As opposed to the first model (Szilard, 1974) this plate is made of a low absorption silicon rubber, again with ten measuring points distributed as before and the thermistors are now embedded in a different, highly absorbant, silicon rubber. The improvement lies in using matched silicon rubbers instead of polystyrene and paraffin wax, giving shorter acoustic wavelengths and no refraction, and the electrical circuit is also improved.

REFERENCE

SZILARD, J., 1974. A New Device for Monitoring Ultrasound Dosage. Proc. 8th International Congress on Acoustics, London (Institute of Physics), p. 352.

POST-MORTEM INVESTIGATION OF B SCAN APPEARANCES OF MALIGNANT LIVER PATHOLOGY

By J. A. King, D. O. Cosgrove, E. Heyderman*, C. R. Hill, S. Pussell and J. Sloane

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Royal Marsden Hospital, Sutton, Surrey

Simple B scans were made of specimens of human liver at post-mortem and were reported blind, by experienced diagnosticians, in respect of the presence and location of metastases. The specimens were then sliced in the scan planes, comparison made with the B-scan, and histology carried out. Of 39 slices covered by the study, 25 were found (retrospectively) to contain metastases and 88% of these were correctly reported from the B scans as being involved, although less than 13% of the individual lesions were correctly identified. Of the remaining 14 sections that did not contain metastases, five (36%) were wrongly reported as positive for involvement.

Histologically, lesions containing large continuous masses of collagen appeared echogenic on ultrasound scans. Some of these showed large central collagenous masses surrounded by peripheral viable tumour; these appeared as "target lesions" on ultrasound scans with their characteristic echogenic centre and relatively anechoic surround. This "target" effect was seen in lesions surrounded by compressed liver cells with sinusoidal dilatation, which corresponded to the outermost anechoic zones of these lesions. Viable tumours, sometimes containing extensive necrosis but without fibrosis, appeared relatively anechoic on ultrasound scans.

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CORRELATION OF HISTOPATHOLOGICAL AND ULTRASOUND APPEARANCES OF LIVER METASTASES

By A. E. A. Joseph, K. C. Dewbury, G. H. Millward-Sadler and C. W. Clarke

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Tremona Road, Shirley, Southampton

Twenty-two livers were obtained at post mortem from autopsies on patients with known primary carcinoma or with secondary deposits noted macroscopically without a past history of carcinoma. Primaries were from nine different sites.

The livers were perfused with normal saline followed by 10% formol saline. Saggital ultrasound scans were done in a water bath at 1 cm intervals and the livers sectioned along the planes of the scans. Photographs were obtained of the macroscopic slices. The number of metastases ranged from 2–30 in each liver. Macroscopic features of metastases were noted and recorded.

The presence of metastatic deposits was detected by ultrasound in 12 cases. There were no false positives and in the one false negative there was diffuse liver involvement with no nodules of over 1 cm in diameter.

Deposits were classified on the basis of ultrasound appearances into non-reflective, reflective and mixed deposits. Target metastases were specifically identified. Sections were obtained for histology from four sites at the peripheries and one from one site in the centre of each deposit. Two hundred and twenty sections were obtained. Sections were also obtained from the non-reflective regions of the target metastases.

Analysis showed that the degree of necrosis correlated best with the patterns of reflection observed. Reflective lesions showed 25% necrosis, non-reflective lesions 75% necrosis, and the mixed lesions 50% necrosis. In all cases the non-reflective halo of target metastases showed histological evidence of marked sinusoidal ectasia. This is at variance with other reports where sinusoidal ectasia had not been identified in target metastases. Acinar formation, mucin production and the amount of fibrous tissue probably influence the appearance of metastatic deposits. This is currently being evaluated. No attempt was made to correlate primary sites with reflective patterns due to the small numbers of each type of primary.

ON-LINE DIGITAL ANALYSIS OF CLINICAL ULTRASONIC DATA

By R. A. Lerski

Department of Radiodiagnosis
Western Infirmary, Glasgow and
Departmen tof Clinical Physics and Bioengineering
West of Scotland Health Boards, Glasgow

A minicomputer-based signal processing system has been assembled for the on-line analysis of clinical ultrasound data with a view to the provision of diagnostically useful parameters regarding tissue characteristics.

A description was presented of the analysis procedures at present in use ranging from simple amplitude and spatial frequency determination to the investigation of the auto correlation function and attempts at deconvolution.

A series of 25 patients with alcoholic liver disease have been investigated and the results of the computer analysis compared with pathological information obtained by needle biopsy. The presence of diffuse disease could be diagnosed correctly in 95% of the cases. Additionally, through the use of a minimum distance classifier, the computer was able to classify the disease state correctly in 72% of the cases.

STATISTICAL VARIATIONS IN ECHO AMPLITUDES AND THEIR EFFECT ON INTERPRETATION OF GREY SCALE IMAGES

By. D. C. Morrison and W. N. McDicken

The Royal Infirmary, Edinburgh

S. R. Wild and W. A. Copland

The Western General Hospital, Edinburgh

Production and interpretation of grey scale images of thyroid and liver were discussed.

Normal liver and thyroid give rise to a range of echo amplitudes resulting in the familiar speckle pattern in the image. The ability to detect an abnormal region within these organs will depend on the size of the abnormality and on how much its echogenicity differs from the normal tissue. Analysis of echo data from livers and thyroids allows an estimate to be made of the effect of the statistical variation of echo amplitudes on the practical resolution obtainable.

These results were compared with analysis of computer synthesized echo data based on a simple tissue model.

PRELIMINARY MEASUREMENTS OF ATTENUATION OF ULTRASOUND IN PLACENTAL TISSUE

By M. Kearle and M. F. Docker

Birmingham University and
Birmingham Maternity Hospital

It is thought that ultrasonic characterization of placental tissue might be of value in certain disease states, for example Rhesus iso-immunization. The placenta has some degree of homogeneity, and it was thought the method used by Mountford and Wells (1972), to investigate the liver might be applicable to the placenta *in vivo*.

Results of these measurements, and of *in-vitro* measurements on the placenta were presented in this paper.

REFERENCE

MOUNTFORD, R. A., and WELLS, P. N. T., 1972. Ultrasonic liver scanning: quantitative analysis of the normal A-scan. *Physics in Medicine and Biology*, *17*, 14–25.

THE VALUE OF REAL-TIME ULTRASOUND IN ABDOMINAL DIAGNOSIS

By H. B. Meire and P. Farrant

Northwick Park Hospital & Clinical Research Centre

Whilst real-time ultrasound has undoubted advantages in the investigation of early pregnancy, its value in abdominal nonobstetric diagnosis has been limited by the relatively poor resolution of current scanners.

We have examined a large series of patients on both a real-time and a conventional "B" scan machine. A wide range of advantages and disadvantages of the real-time system have become evident and were presented. Also presented were a number of cases in which real-time ultrasound permitted the diagnosis to be reached after conventional "B" scanning had failed.

THE SIGNIFICANCE OF ULTRASONIC GALLBLADDER WALL THICKENING

By R. C. Sanders and E. Zerhouni

John Hopkins Hospital, Baltimore, USA

The thickness of the gallbladder wall has been measured on 300 gallbladders, fifty with proven gallstones. In 250 there was no evidence of gallbladder pathology. Gallbladder wall thickening was as common in patients without symptoms as in those with cholecystitis. Echogenic gallbladder wall thickening was found to be of no pathological significance. Patients with alcoholic liver disease were noted to have gallbladder wall thickening more frequently than others. This was particularly noticeable in patients with ascites.

In patients with acute cholecystitis, a minority showed a form of gallbladder wall thickening in which there were decreased echoes within the gallbladder wall. In three patients with hyperplastic cholecystosis there was irregular gallbladder wall thickening with polypoid protrusions into the gallbladder lumen.

GREY-SCALE ULTRASONOGRAPHY AND ENDOSCOPIC PANCREATOGRAPHY IN PANCREATIC DIAGNOSIS

By W. R. Lees

Middlesex Hospital, London

Grey-scale ultrasonography (US) and endoscopic pancreatography (ERCP) have been compared in a consecutive series of 216 patients. The overall results were remarkably similar, and the two techniques gave complementary information. US failed to give adequate views in 13 cases, and pancreatography failed in ten. In all 60 cases already known to have pancreatitis US accurately documented the presence or absence of cysts. ERCP mapped the duct systems and revealed many congenital anomalies of the pancreas. In 33 patients with relapsing acute pancreatitis, ERCP was normal in 19 and US in seven. Both techniques demonstrated gall-bladder stones which had been missed on previous orthodox radiology.

One hundred and fifty-six patients presented as problems in diagnosis; the final conclusion after full investigation was: cancer (22), pancreatitis (17), normal pancreas (82); the 35 other patients were also believed to have a normal pancreas, but some doubt remained. There were no normal ERCP or US reports in patients with cancer, but two of the US reports wrongly favoured pancreatitis. In the 82 patients with a normal pancreas, ERCP gave three false positive reports, and US wrongly reported cancer on four occasions and pancreatitis once.

A normal ultrasound scan virtually excludes pancreatic disease and no further investigation is necessary unless clinical suspicion is high. The combination of US and ERCP provides accurate and rapid pancreatic documentation.

THE ULTRASONIC DEMONSTRATION OF HUMAN FOLLICULAR AND CORPUS LUTEUM DEVELOPMENT: A NEW METHOD FOR OBSERVATION OF OVARIAN DEVELOPMENT

By B.-J. Hackeloer

Universitats Frauenklinik & Hebemmenlehramstadt
Marburg, West Germany

The use of ultrasound as a routine examination in obstetrics is well known. In gynaecology it is often limited to diagnosis of abdominal masses. Detailed systematic studies of the normal ovary using ultrasound are lacking and are limited to two or three reports, including work on the "stenoid" ovary.

The accurate assessment of follicular growth and development is important in the investigation and treatment of the infertile woman. In such patients it is essential that the techniques employed are non-invasive and have no potential for causing harm to an early conceptus. In 1975 we studied first patients undergoing stimulation of ovulation with gonadotrophin therapy. Using the full bladder technique, the ultrasound examination allowed visualization of the developing cystic structure of the ovary, determination of the presence, number and size of follicles. The results of 250 such scans in some 20 cases allowed us to deduce that ovulation induction would be successful (as shown by subsequent pregnancy) if the follicular diameter lay between 18 and 23 mm. The technique could also be a value by determining the presence of multiple follicular development and consequently the risk of resultant multiple pregnancy and hyperstimulation.

We are studying now spontaneously ovulating patients in the same way because previous workers have suggested that the follicular size at the time of spontaneous ovulation is 13–15 mm. Human follicular development measured by peripheral plasma hormone levels and ovarian follicular growth assessed by ultrasound were compared. The linear correlation coefficient between the mean values for plasma estradiol and follicular diameter on days −5 to day 0 was r=0.968, and the diameters found were similar to data presented above.

It seems that ultrasound measurement of follicular diameter offers an additional technique for the study of ovarian function.

CARCINOMA OF THE OVARY—CORRELATION OF ULTRASOUND AND X-RAY COMPUTED TOMOGRAPHY WITH SECOND LOOK LAPAROTOMY

By S. J. Pussell, D. O. Cosgrove, E. Wiltshaw, J. Hinton, G. H. Barker and Janet E. Husband

The Royal Marsden Hospital
Downs Road, Sutton, Surrey

In a series of patients with carcinoma of the ovary, results of ultrasound examination of the pelvis and abdomen and results of X-ray computed tomography (CT) of the pelvis were correlated with second look laparotomy. Strict criteria apply to selection of the two groups of patients submitted to second operations. In the first group, patients have stage III or IV disease, have been on chemotherapy for five to seven months and have responded to treatment according to clinical assessment. The second group have had carcinoma of the ovary treated previously with surgery, radiotherapy and/or chemotherapy and clinically have recurrent disease. The second operation is primarily a debulking procedure where as much residual tumour as possible is removed. Pelvic structures not removed at primary surgery are also excised. Second look laparotomy offers an ideal opportunity to test the accuracy of ultrasound and CT in detecting disease.

A standard technique is used for ultrasound scanning. The patient is required to have a full bladder and an empty sigmoid colon and rectum. Diuretics and aperients are used when necessary. The liver, mid abdomen, para aortic region, pelvis and kidneys are scanned routinely with single pass B scans, using a high resolution grey scale machine at 3 MHz. Computed tomography is performed on an EMI CT 5005 body scanner and transverse tomograms are produced at 1.5 cm intervals throughout the pelvis. The patient is required to have a full bladder. Gastrografin (sodium diatriozate) 5% contrast medium is used in the lower bowel. Buscopan (hyoscin-N-butyl-bromatum) 20 mg is given intramuscularly and a vaginal tampon is inserted for all pelvic examinations.

Twenty-six patients have been studied to date. Ultrasound was performed in all patients and CT in eleven patients. Ultrasound was sensitive in detecting recurrent tumour in the pelvis and metastases in and around the liver. CT was not as accurate as ultrasound in the pelvis. Ultrasound consistently failed to detect intraperitoneal seedlings except when disease was gross and/or ascites was present. This is to be expected as the size of most peritoneal deposits is beyond the resolution of both modalities. These lesions however are easily detected at laparoscopy.

RADIAL SCANS OF THE EXTRAHEPATIC BILIARY SYSTEM IN OBSTRUCTIVE JAUNDICE

By J. G. Duncan

Royal Infirmary, Glasgow

The ability of ultrasound to differentiate between obstructive and non-obstructive jaundice is well recognized and is a useful selective method for further investigation. This may take the form of percutaneous transhepatic cholangiography either alone or in conjunction with endoscopic retrograde choledochopancreatography. However, ultrasound may give useful information about the level and cause of obstruction in obstructive jaundice.

A dilated extrahepatic biliary system may be difficult to distinguish from the portal vein. The anatomical relationship of these structures may be demonstrated and identified by radial scans of the extrahepatic bile ducts. Clear definition of the neck of the gallbladder may also be obtained. The level of obstruction and, in some instances, the cause may be assessed with some accuracy.

In a recent series of 43 patients with surgical jaundice, ultrasound detected the level of the obstruction in 28 cases, the level being identified in 70% of cases of malignant obstruction and in 55% of gall stone disease. Gall stones were identified in the common bile duct in only 15% of cases proven at operation. Of seven patients with proven carcinoma of pancreas five were detected by ultrasound.

A PROSPECTIVE STUDY OF THYROID ULTRASONOGRAPHY

By W. R. Lees, L. R. Watson
and R. C. G. Russell

Departments of Radiology and Clinical Measurement
Middlesex Hospital, London

The management of thyroid swellings has become more controversial since the spread of ultrasonography for the diagnosis of thyroid lesions. Apart from the case of simple cysts, the diagnostic accuracy is only now reaching the level at which the clinician takes notice.

We report on the use of ultrasonography in 141 patients in whom a final diagnosis has been obtained. Ninety of these had a histological, and 51 a firm clinical diagnosis. The ultrasonographic features of thyroid disease and criteria for diagnosis are described.

Local and general disease was correctly distinguished in 96% of the cases. Only one truly solitary lesion was not interpreted as such (a solitary adenoma was described as a multiple adenoma). Most of the diagnostic problems encountered in making this distinction have arisen from the misinterpretation of the dominant nodule in a multinodular goitre.

The overall accuracy in providing a tissue diagnosis was 86% (simple cysts (16) 100%, adenomas (33) 88%, colloid goitres (44) 77%, the thyroidites (22) 82%).

The anatomy and pathological changes in the gland were nearly always correctly described. Most errors were those of interpretation, engendered by the variability of pathological change in thyroid disease.

Twenty-seven patients presented an appearance suspicious of malignancy. All nine of the thyroid cancers were placed in this category, although only four were confidently diagnosed as such.

The role of ultrasonography in the management of thyroid disease was discussed.

Forthcoming events

The editors have decided to accept requests for meeting announcements by organizations other than The British Institute of Radiology and its associated bodies on the basis of charging at £1·00 per line per edition. Copy deadline for inclusion in this section is the 20th of penultimate month preceding publication (*i.e.* April 20, for June edition).
Requests should be addressed to Mrs. L. Surry, Managing Editor, The British Journal of Radiology, 32 Welbeck Street, London W1M 7PG.

Intensive Course in Medical Radiation Biology and Medical Statistics

An intensive five day course, suitable for candidates preparing for the first examination for the R.F.C.R. (and the D.M.R.T.) will be held at Ruchill Hospital, Glasgow, where residential accommodation is available on June 11–15 1979.

The course has been designed to cover the syllabus in both medical radiation biology and medical statistics as required by The Royal College of Radiologists for its first examination in radiotherapy.

Course fee: £75.

Course Organizers: West of Scotland Committee for Postgraduate Medical Education (in association with The Glasgow Institute of Radiotherapeutics and Oncology).

Further details and application forms may be obtained from: Dr. J. Kirk, Radiobiology Research Group, Glasgow Institute of Radiotherapeutics and Oncology, Belvidere Hospital, Glasgow G31 4PG.

Nuclear Cardiology

A workshop organized by the Nuclear Medicine Committee of The British Institute of Radiology to be held on June 20, 1979 at St. Bartholomew's Hospital, Gloucester House, Little Britain, London EC1. Anyone wishing to make a presentation should contact Dr. K. E. Britton, St. Bartholomew's Hospital.

Further information regarding this meeting can be obtained from the General Secretary, The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG (01-935 6237).

18th Congress of the Society of French Speaking Hospital Pysicists

The 18th Congress of the Society of French Speaking Hospital Physicists will take place in Nancy (Centre Alexis Vautrin) on June 21–23, 1979.

Scientific programme: The combination of external radiotherapy and curietherapy in the treatment of head and neck carcinoma; measure of low dose in radiodiagnosis and radiotherapy; inhomogeneities in radiotherapy (photons and electrons).

Further information from the Secretary, Melle Roy, Congress SPHEF, Centre Alexis Vautrin, R.N. 74-Brabois, 54500, Vandoeuvre-les-Nancy. Tel: (83)-55-81-66, ext. 283.

European Symposium on Radiopharmacology

To be held at Noordwijkerhout (The Netherlands) June 21–23, 1979.

This symposium will be held under the auspices of The European Nuclear Medical Society, The Society of Nuclear Medicine (Die Gesellschaft für Nuklearmedizine) and The Department of Nuclear Medicine Rotterdamsch Radio-Therapeutisch Instituut, Groene Hilledijk 301, 3075 EA Rotterdam, Head of the Department: Dr. P. H. Cox.

Sessions will be held on ionic tumour localizing radiopharmaceuticals, technetium Hida derivatives for liver function investigations and technetium skeletal scanning reagents.

For further details and registration please contact: Dr. P. H. Cox, Head of Department of Nuclear Medicine, R.R.T.I. Rotterdam: Groene Hilledijk 301, 3075 EA Rotterdam, The Netherlands.

20th Summer School in Health Physics

This course being held July 2–13, 1979, provides a broad background in the subject and is particularly suited to those carrying responsibilities for radiological protection in government, industry, hospitals and education.

Details from Dr. H. D. Evans, Health Centre, Imperial College, London SW7 2AZ.

Recent Advances in Ultrasound

This is a day meeting at Addenbrookes Hospital, Cambridge, on Wednesday, July 11, 1979

Speakers will include Dr. M. Bark, Mr. R. Blackwell, Dr. L. Burger, Dr. D. Cosgrove, Dr. C. Metrewelli and Dr. W. R. Lees.

Closing date for applications: June 25, 1979.

Further details from Meeting Organizer, Dr. J. Tudor, Department of Radiology, Addenbrookes Hospital, Cambridge (tel.Cambridge 45151, ext. 203).

IV European Congress of Radiology

The IV European Congress of Radiology will take place in Hamburg (German Federal Republic), September 4–8, 1979.

Scientific programme:
diagnostic research of organs of the upper abdomen;
diagnostic research in nuclear medicine: organs of the upper abdomen;
radiotherapy in tumours of the genital system of males and females;
radiobiology and X-ray protection (combined therapies and risks of ray exposure);
radiophysics and techniques (methodical problems in diagnostics and in planning of radiotherapy).

Enquiries: Secretary of the IV European Congress of Radiology, Postfach 10 64 07, D-2000 Hamburg 1, Federal German Republic.

Hyperthermia in Radiation Oncology

First European Meeting under the sponsorship of the European Organization for Research and Treatment of Cancer (EORTC) Radiotherapy co-operative group will be held on September 10, 1979 (the day before the Gray Conference) at St. Catherine's College, Cambridge.

Deadline for abstracts: June 30, 1979.

Details and forms may be obtained from Dr. G. Arcangeli, Istituto Medico Scientifico, Clinica Villa Flaminia, Via Luigi Bodio 58, 00191 Rome, Italy.

Quantitation of Tumour Response: a Critical Appraisal

The L.H. Gray Conference will be held in Cambridge, England, during the week of September 10–14, 1979. The topics of the meeting are intended to stimulate a critical appraisal of the techniques that are currently in use both experimentally and clinically for assessing tumour response after therapy. The topics will include:

In situ measurements of tumour response, including improved methods of tumour detection in clinical studies.
Factors of prognostic significance.
In vitro assays of tumours excised after treatment *in vivo*.
The choice of suitable experimental models in rodents.
The role of human tumour xenografts.
Statistical evaluation of tumour response data.
The limitations and artefacts of each assay technique.
The relationship between cell survival and the *in situ* response.

Further information from Dr. J. Denekamp, Gray Laboratory, Mount Vernon Hospital, Northwood, Middlesex, England.

Recent Advances in Brain Scan

Bordeaux, September 20–22, 1979. Under patronage of Université de Bordeaux II and Institut National de la Santé et de la Recherché Médicale (INSERM), Professor J. M. Caille and G. Salamon are organizing in Bordeau a meeting devoted to "Recent Advances in Brain Computed Tomography".

Subjects: Physical basis of computed tomography by transmission; normal and pathologic results and their correlation. Other methods of tomography (neutron scanner, emission scanner, etc.).

The languages used will be French and English. Fees: 500 F.F.

For any information: Professor Caille, Service de Neutroradiologie, Hôpital Pellegrin-Tripode, 33076 Bordeaux. Tel. (56) 96 83 83, poste 4603.

5th International Congress of the International Radiation Protection Association

Will take place in Jerusalem, Israel, March 9–14, 1980.

The scientific programme of the Congress will cover all aspects of radiation protection with emphasis on its central theme: radiation protection—a systematic approach to safety.

An interesting programme has been planned including a commercial exhibition and pre- or post-congress workshops and Professional tours.

Social events and a programme for accompanying persons have been organized.

For further information: The Secretariat, 5th International Congress of IRPA., PO Box 16271, Tel Aviv, Israel.

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Symposium on Spine and its Contents

EAR "Symposium Vertebrologicum" (Spine and its Contents) will be held from April 23–25, 1980 in Prague, Czechoslovakia.

The subjects of this symposium will be recent advances and experiences in:

(a) Equipments and investigative methods of spine and spinal cord.
(b) Radioanatomy and physiology of spine and spinal cord.
(c) Radiodiagnosis of pathological conditions.
(d) Interventive (diapeutic) radiodiagnostic methods.

For further information contact (not later than June 1979): The secretariat of "Vertebro 1980", PO Box 88, Sokolská 31, 120 26 Praha 2, Czechoslovakia.

XV International Congress of Radiology

The XV International Congress of Radiology will take place June 24–July 1, 1981 in Brussels, Belgium.

The scientific activities of the Congress as well as the scientific and technical exhibitions will take place in the Brussels Exhibition Centre.

Further information from: Secretariat ICR-81, Ave. Winston Churchill 234B-Box 16, B-1180 Brussels, Belgium.

Book reviews

Surface Anatomy for Radiographers. By D. W. McKears and R. H. Owen, pp. 105+index+10 illus. 1979 (Bristol, John Wright & Son), £4·00.
ISBN 0-7236-0511-4.

This small book fills a large gap in bringing together all the information about surface anatomy which our students are expected to know.

The book is divided into two sections: the first on the surface anatomy of the bony structures and the second on the soft tissues, and it sets out clearly and simply the relationship between the two.

There are clear line diagrams on nearly every page and it is beautifully illustrated with ten photographic plates of various well known statues mostly showing muscles.

The book has an appendix giving a very simple summary of planes, landmarks and structures at every vertebral level, and an introduction describing, among other introductory comments, methods of palpation and visual inspection which very few books available to the radiography student include.

At £4·00, this little book would be a useful addition to every radiographer and student radiographer's private collection, particularly those specializing in ultrasonics. It could also be a useful reminder to radiologists.

Jennifer Richmond.

Normal Radiologic Patterns and Variances of the Human Skeleton. An. X-ray atlas of adults and children. By R. Birkner, pp. x+564, illus., 1978. (Urban & Schwarzenberg, Germany), DM 148.
ISBN 0-8067-0211-7

This is an encyclopaedia of the normal bony skeleton and its variants, printed in Germany. It is beautifully illustrated on high quality paper with over 800 very fine positive print radiographs and approximately 400 line drawings.

There is a short initial chapter on X-ray physics, radiography and protection. The adult skeleton is demonstrated with great care and thoroughness and its variants described. I very much appreciated the use of dried skull sections in explanation of tomographic anatomy and the radiographs of the variants of the sella turcica. There are short sections on idiopathic scoliosis and double contrast knee arthrography.

To complete the book there is a very substantial chapter covering the difficult subject of the skeleton in childhood and adolescence and this is particularly valuable. The references are refreshingly European.

The quality of this book is unmistakable. It should become, an essential reference book for all undergraduate libraries, orthopaedic surgeons and radiologists.

A. B. Ayers.

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The diagnostic limitations of computerized axial tomography 443

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Tactics and strategy in cancer treatment 511

Surface anatomy for radiographers 522

Normal radiologic patterns and variances of the human skeleton. An X-ray atlas of adults and children 522

Books received

Receipt of the following books is acknowledged as a courtesy to the sender.

Clinical applications of the electron beam. Edited by Norah du V. Tapley, pp. xiii+274, 1976 (John Wiley & Sons Ltd., Chichester) £15·00.

High-energy photons and electrons: clinical applications in cancer management. Edited by S. Kramer, N. Suntharalinger and G. F. Zinninger, pp. xi+363, 1975 (John Wiley & Sons Ltd., Chichester), £17·65.

Computers in the Control of Treatments Units

The British Institute of Radiology: Special Report No 16, March 1979

by R. E. Bentley, A. L. Bradshaw, C. A. F. Joslin, W. J. Redmond, M. E. Rosenbloom, B. J. Scholl-Evans, J. B. H. Stedeford and R. C. Tudway.

Digital computers are being used very successfully in radiotherapy dose computation. This report deals with another, at present less highly developed, application of computers, the provision of some degree of automation at the point of treatment. Drawing on their own practical experience, on information from manufacturers and on the relatively sparse literature on this topic, the authors analyse the reasons for wishing to introduce some automation, discuss suitable techniques and procedures and make specific recommendations. Practical problems in implementing such control systems, including the need to gain acceptance from those operating the equipment and from those being treated, are carefully considered.

The authors were of a multidisciplinary Task Group, convened by Dr. Roy Bentley, which had been set up by the British Institute of Radiology Working Party on "Applications of Modern Technology in Radiotherapy."

The report should be of interest to all those concerned as users, designers or manufacturers with future developments of radiotherapy apparatus.

Orders to:
The British Institute of Radiology, 32 Welbeck Street, London W1M 7PG

or through your bookseller Price: £2·40
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